STUDY OF VAGINAL CYTOLOGICAL CHANGES BEFORE AND FOLLOWING DIFFERENT METHODS OF CONTRACEPTION

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FOR

MASTER OF SURGERY

(OBSTETRICS & GYNAECOLOGY)

BUNDELKHAND UNIVERSITY
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TRIPTA SHRIVASTAVA

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C E R T I F I C A T E

This is to certify that work on 'STUDY OF VAGINAL CYTOLOGICAL CHANGES BEFORE AND FOLLOWING DIFFERENT METHODS OF CONTRACEPTION', by Dr.Gupta Shrivastava has been done in the Department of Obstetrics and Gynaecology, M.L.B.Medical College, Jhansi under my guidance and supervision.

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30th May, 1983

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INTRODUCTION

INTRODUCTION

The average life expectancy has increased, and the infant mortality rate has decreased due to the scientific advancement made for the protection, care and health of the man. But now the population is increasing in huge numbers. The rate of increase is such that whereas it took 200 years for the population to double between A.D. 1650-1850, it is realibly predicted that doubling of the number now on the earth will take only 30 years and the next doubling there after in an even shorter period. Particularly, this is true for the developing countries leading to serious problems, which have been created by progress and at the same time, by the Socio-economic injustice existing between the able world and the overpowered world, between the giant, economically developed nations and the developing countries who are struggling for life and for social and economic freedom.

The problem of population control is at its brim of explosion and it is causing concern to all countries in the world. India, unfortunately is affected the worst, because of a very high birth rate. Inspite of the increase in the resources, it is impossible to cope up with the rising population because such a phenomenon occurs in a geometric progression. India possibly is the country which has taken Family Welfare Programme on a Government level. The administrator social worker, economist and the Medical man have all joined together to face and solve the difficult task.

There is no doubt, that a programme of this magnitude can not succeed unless the desired emphasis is not given on each method of family limitation. Fortunately, today such an attitude has been adopted by our experts and administrators.

During the past decade, great advances have been made in contraceptive technology. Apart from conventional contraceptives, namely condom with or without spermicidal jelly, the widespread use of newer contraceptives specially the

systemically acting steroids have evolved. The development and subsequent modification of oral contraceptives together with the designing of improved type of Intrauterine Contraceptive Device has radically altered the contraceptive practice of couples throughout the world.

Intrauterine devices have an important role to play as a method of family spacing in the National Family Welfare Programme of our country. Of all the contraceptive methods developed in the past, perhaps the most widely used is the Copper Intrauterine Device. Copper metal with biologic substrates is highly active and Copper ions which are liberated inhibit the implantation of ovum.

Existing clinical data concerning the efficacy of intrauterine contraception have pointed to certain limitations for wide scale application of this type of fertility control. The principle clinical factors which govern their use effectiveness, were menorrhagia, pain, expulsion and accidental pregnancy. By analysis of the data collected by Tietze in the Co-operative Statistical Programme (1968), it appeared that the degree to which one or another of these complications occurred depended considerably upon certain physical properties of the devices and duration. Correlation of the certain characteristics and the related clinical manifestations permitted the development of certain guide-lines which can be used to predict the clinical efficiency of an intrauterine contraceptive device. These guide lines are as follows:-

(a) Rate of accidental pregnancy is inversely related to the endometrial surface covered by the device in the area of normal implantation.

(b) The occurrence of menorrhagia and pain have a direct relationship to the area of endometrium in contact with the device, and to the pressure which the device exerts upon the endometrium and the myometrium.

(c) The rate of first expulsion is inversely proportional to the stiffness of the device in those instances when the retention was governed primarily by the resiliency of the device.

During the past decade there has been a change in the medical attitudes towards contraceptive techniques resulting in a transition from concentration on vaginal methods to the development of measures using the constitutional approach, which theoritically, have widespread effects in various areas of the body.

The new approach eventuated some years back in the initiation of first clinical trials of oral contraceptive preparations employing gonadal type hormones for the primary purpose of inhibiting ovulation in otherwise normally ovulating women. In 1956, the first trial of this type began in San Juan, Puerto Rico, by Pincus etal, and Tyler and his colleagues.

It is generally believed that the currently available oral contraceptives are virtually 100 percent effective if taken daily from 5th to 25th day of the cycle. The higher degree of effectiveness is attributable to inhibition of ovulation and two other factors:

Factor (1):

Attention of the cervical mucus, so that sperm penetration is inhibited, because of the change in the mucus from the normal thin, glary, watery type of the thick viscous mucus type usually seen quite late in the cycle.

Factor (2):

Use of endocrine substances has altered the endometrium so that it became unsuitable for nidation, as the glands became quite atrophic while the stroma is quite loose. This type of contraception is associated with side effects like withdrawl bleeding, break through bleeding, and hormonal disturbances. Fertility, returned promptly after cessation of contraception.

The effectiveness of hormonal contraception has been fully established in the last 15 years but the method to be successful requires a high degree of motivation to ensure regular pill taking.

The widespread use of oestrogen progestin combinations for contraceptive purposes or for the treatment of various gynaecological disorders have produced novel endometrial patterns which have been extensively studied and described. Hormonal medication for contraception has been used by increasing number of women, since 1956 in developed countries.

In the past few years, cellular abnormalities have been observed in smears from the genital tract of some patients who received Oestrogen-progestin compounds. From random observations, it appears that a typical cells are seen with greater frequency and in a younger age group among women receiving the compound than among the non-medicated patients.

The growing acceptance of various oral contraceptive agents have created extensive controversy concerning both the immediate and delayed effects of these preparations. Several reports of an increase in incidence of cervical pathology, particularly dysplasia after the use of oral contraceptives has appeared in recent years. The relationship of the steroid hormones to the pathogenesis and progression of cervical cancer has been poorly understood. Some authors have reported that oral contraceptives have no relation to cervical cancer. (Weid etal, 1966, Secost and Baier 1967), while on the other hand there are reports which indicated higher incidence of cervical carcinoma among women using oral contraceptives (Taylor 1967, Graham etal 1968). Abnormal cytological findings such as enlarged nuclei, hyperchromatic and nuclear irregularities have been reported in women using oral contraceptives as compared to controls (Cohr, 1966, Liu, etal 1967) emphasized that ovulation inhibitors induce changes in the squamous epithelium of portio vaginalis in every case varying however in severity.

The oral contraceptives now used are composed of synthetic oestrogens and progestagenes. They effect the endometrium and the vaginal epithelium which are both easily accessible organs.

With a prolonged history of oestrogen therapy, there is presence of all intermediate patterns from simple cystic, hyper plasia through more proliferative adenomatous hyperplasia to the production of frank unquestioned corpus cancer. This has been repeatedly observed by interested pathologists since the initial articles by Taylor (1932), and Novak and Yui (1936). Simple cystic or proliferative hyperplasia may be found in conjunction with frank cancer and all gradations may occur. Finally, it must be emphasized that the role of oestrogen in the development of endometrial Cancer is still speculative.

Vaginal Cytology is the simplest parameter which can explore the possibility of some most important complications namely pelvic infections, dysplasia and genital malignancy developing after prolonged use of modern contraceptives. The present study has been carried out for the identification of incidence of these complications following the use of conventional contraceptives, IUCDS and oral pills.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

BRIEF HISTORY :

INTRA UTERINE CONTRACEPTIVE DEVICES:

The idea of contraception is not new and it has a history of some five thousand years. The use of an intra uterine contraceptive device was also not a new concept, although revival of interest in its application was very recent.

Ancient Arbs used a small round, smooth pebble introduced by means of a hollow tube into the uterus of the camel to prevent conception.

In 1909, a report describing a practical intrauterine device appeared for the first time in a German Medical Journal. (Kleinman, R.L. 1937). The article by Richard Richter described his use of a flexible ring of silkworm gut. He had placed these rings in the uteri of women seeking contraceptive help in his medical practice at Waldenburg, near Breslau, in present day Poland.

The best known name in the history of Intra Uterine Contraceptive Devices is that of Ernst Grafenberg 1929. He claimed that the only way to prevent ascending infection associated with the stem pessaries then in use was to put a device wholly within the uterus.

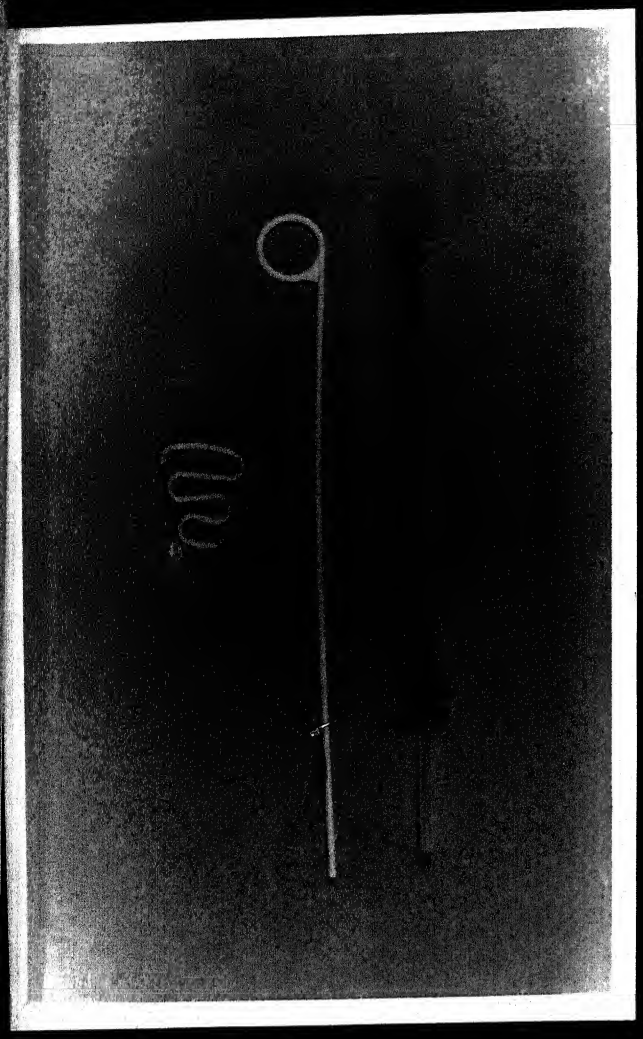
In 1959, Oppenheimer of Israel described his 20 years experience with various Intrauterine Contraceptive Devices. And in the same year, Ishihama from Japan reported the use of Ota Ring (developed in 1934) in over 20,000 women. Both these reports had described low pregnancy rate, the absence of serious side-effects and minimal chances of pelvic infection.

So the interest in Intrauterine Contraceptive Devices research was renewed around 1960 partly due to the facts mentioned above and partly because of three important events which are:-

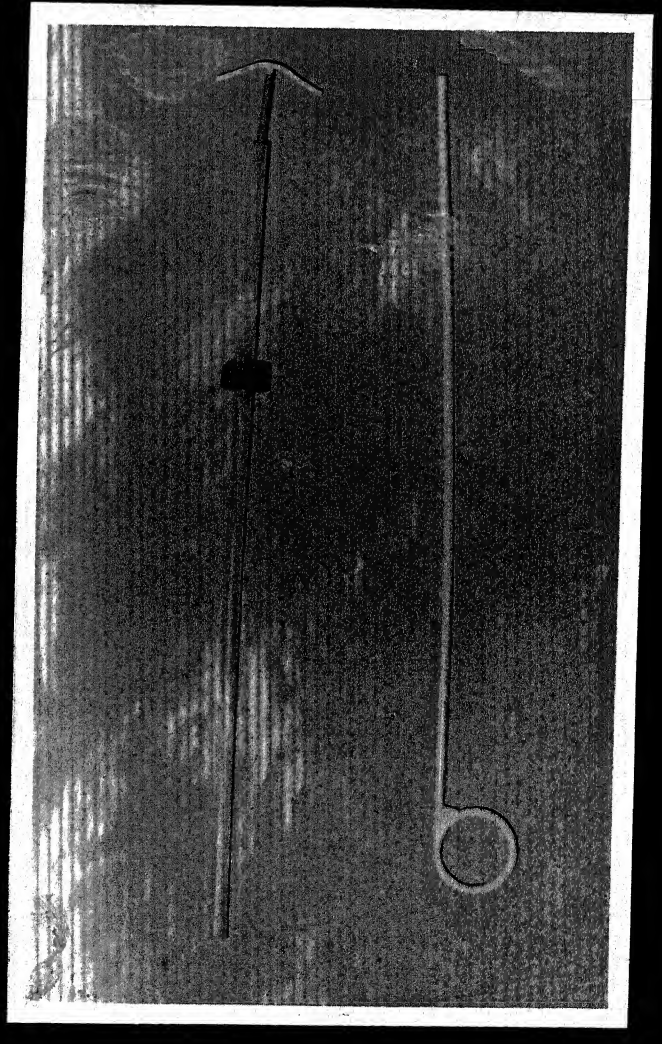
1. Realization of population explosion.
2. Availability of biologically inert material.

PHOTOGRAPHS

Photograph showing - Hypos Loop.



Photograph showing Copper 'T'



3. Advent of antibiotics.

The modern area of Intrauterine Contraceptive Devices started in 1962 by the Population Council and objective international appraisal of Intrauterine Contraceptive Devices was planned. In 1962, the first International Conference on Intrauterine Contraception was held in New York, and it was found that there was no evidence of carcinogenic effects and that there was no impairment of fertility after the Intrauterine Contraceptive Device removal following prolonged use.

The Hall Stone Ring (a modified Grafenberg Ring) which was introduced for the first time was made of Stainless Steel.

Also by 1962, Margulies Spiral was also introduced in the same Conference. Again 1962, technological advances had led to the development of a biologically inert plastic material that could be easily and precisely molded and Lippes introduced the first modern Intrauterine Device. Lippe device (Fig. 1) had two improvements:

1. a transcervical tail or thread to assist in its removal and to help in self examination and
2. barium sulfate to make the Intrauterine Device radio-opaque and thus easy to localize.

In 1964, Second International Conference took place.

In view of the complications such as bleeding, cramps and expulsion, the first medicated devices (Copper 7 and Copper 'T') were developed by Tatum and Zipper and their co-workers (Fig. 2). Pandya and Scommegna published the first clinical trial on hormone releasing intrauterine devices in 1971.

Till 1980, innumerable symposia had been held on the subject of intrauterine contraception. It was estimated now that approximately 50 to 60 million devices were in use all over the world.

ORAL CONTRACEPTIVES:

The advent of oral contraceptives during the 1960s

had been one of the significant advances of modern science. The drugs became a reality at a time when many individuals were aware of the 'Population explosion' and have influenced family planning programme in many parts of the world.

It was postulated as early as 1897 by Beard in Edinburgh, that the corpus luteum of the ovary which secretes progesterones, was responsible for the inhibition of ovulation during pregnancy. This concept was support by Pennant in Nancy in 1898.

However, it was Professor Ludwig Haberlandt of Innsbruick, who first advocated the use of ovarian and placental hormones for fertility regulation both in animals and in women. A detailed account of these studies was published in 1924.

At this stage, as so frequently in history, Hungarians appeared on the scene. Haberlandt initiated a collaboration with the Gedeon Richter Company of Budapest and hoped that such a hormonal product, called Infecundin, could be marketed soon, but his death in 1932 put an end to this endeavour.

However, it still took almost 18 years before Pincus at the 5th International Planned Parenthood Conference in October 1955, demonstrated, that progesterone inhibits ovulation also in women, when administered in large doses.

The development of a new progestin for use as an orally effective contraceptive was dependant on several factors.

(1) the concept that such a hormone can be expected to control ovulation.

(2) the synthesis of potent orally active progestins.

(3) the biological evaluation and selection of the new steroids for clinical testing, and

(4) the demonstration that the compounds were both effective and safe in women.

The story starts when Margaret Sanger and Mrs. O. Mecormick, two ladies with an important place in history

persuaded Pincus to start a screening programme of contraceptive steroids in animals, the first rabbit experiment was carried out by M.C.Chang on April 25th, 1951 and these studies were published in 1953.

Paper of Rock, Garcia and Pincus demonstrating the contraceptive effectiveness of norethynodrel in women, was published in 1956.

The evaluation of Enovid (the combination of norethynodrel and mestranol) for control of ovulation continued to expand. A large scale study of Enovid was initiated at the Los Angles planned, Parenthood Centre by Dr. Edward Tyler in 1956 and additional studies were undertaken in Puerto-Rico and Haiti by Pincus, Garcia, Rock, Cook, Satterthwaite and Gamble and Safety continued to be demonstrated towards the end of 1959. Enovid was approved for use as an oral contraceptive. Such is the brief history of the first oral contraceptive to be developed for family planning purposes. U.S.Food and Drug Administration approved Enovid for menstrual regulation in 1957 and for contraception in 1959.

Tyler 1961, then made extensive studies on the contraceptive effectiveness of norethindrone but these studies were made without added oestrogen.

These and other studies led to the development of norethindrone as Norlutin, a new progestin for the treatment of menstrual disorders and as an oral contraceptive in 1962. Rock etal also found that norethindrone along with norethynodrel effectively inhibited ovulation in women.

The first reports on the use of norethyndrone in combination with mestranol were published by Goldzeiher etal and Rice-Wray etal in 1962, and was shown to be effective and safe for family planning purposes. It was reported for use in Medical practice as Ortho-Novum in 1961. Thus, a second oral contraceptive was made available.

Pincus in 1965 described his studies in a broader content.

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. group of contraceptive steroids consists of ...gues of 17 acetoxy progesterone, such as medroxy progesterone acetate, megesterol acetate and chlormadinone acetate.

Finally, a third and most potent type of compound developed belonged to the family of 18-Nore-steroids and indeed one of these, levonorgestrel is considered to be the most successful progestrogen synthesized so far.

Further more, the dose of steriod administered has been gradually reduced during the past decade by the systematic efforts of Chinese investigators Briggs and Diczfalusy in 1974 to develop their Pill No. 1 containing 0.625 mg norethisterone with 0.035 mg ethynyle + radiol.

Table 1 shows steriod load represented by a modern pill is approximately 2% of that of the original Enovid formulation.

Table 1 : The daily steroid load of oral contraceptive in 1959 and 1979.

	1959	1979
Progesterone	Norethynodrel	Levonorgestrel
Dose	9.85 mg	0.15 mg
Oestrogen	Mestranol	Ethynlestradiol
Dose	0.15 mg	0.03 mg

According to Landgreen and associates (1979) number of vaginal devices releasing constant small amount of progestogens have reached the stage of indepth clinical testing.

As a more recent development, Chinese investigators, Hsiao Pilien (1977) were studying a number of orally administered formulations which interfere with fertility when given in relatively large doses during a period of fourteen days at any time in the cycle, as so called 'home-visiting' or 'vacation-pill'. These pills do not contain any oestrogen.

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MODE OF ACTION

INTRAUTERINE CONTRACEPTIVE DEVICES :

Despite the wide use of intrauterine contraceptive devices for more than two decades and despite the intensive research works, the precise mechanism of contraceptive action remains not very clear. Many hypothesis had been suggested but none of them could give a satisfactory explanation.

One of the most widely accepted theory given by Gupta etal (1971), Moyer and Mishell (1971), Sagizoglu (1971) was that all the Intrauterine Contraceptive Devices, unmedicated as well as medicated, stimulated in inflammatory foreign body reaction in the uterus. Numerous polymorphonuclear leucocytes appear in the endometrium and uterine fluid, followed by foreign body giant cells, mononuclear cells, plasma cells and macrophages. These cells may engulf or consume the spermatozoas or the fertilised ovum by the process of phagocytosis. But in primates and human beings, this theory no longer seems relevent according to Zipper etal (1977).

The increased contraceptive effiency of copper had been considered to result from-

1. Biochemical and morphological reactions of uterine and oviductal mucosa, which inhibited implantation of ovum as stated according to Chang and Tatum (1970) and Nagenfeldt (1972).
2. Direct influence on the blastocyst (Haaslund, 1972).
3. Spermatocidal effect (Macleod,1951).

All the hypothesis available upto now can be included in one of the above mentioned groups.

It had been reported by Nagenfeldt (1972), that the endometrial concentration of Zn decreased in presence of Cu-device and that copper strips inhibit the activity of some Zinc dependent enzymes such as alkaline phosphates and Carbonic anhydrase.

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Hicks etal (1975) described that addition of copper to the devices resulted in significant changes in the ionic composition. Adequate ionic enviorment in tissue was related to enzyme activity, but it was also important for nuclear acid stability and for the appropriate functioning of the mechanism of protein synthesis.

Main changes observed in the endometrium by Hicks etal (1975) were a significant decrease in the content of RNA in both phases of the menstrual cycle, a significant decrease in protein in the secretory phase and drastic changes in the fucose sialic acid ratio which decreased during the proliferative and increased during the secretory phase.

According to Hicks and Hernandez (1975) the normal human secretory endometrium contained 4.86 ± 0.28 mg Ribonucleoprotein particle per gram wet weight, while the endometrium of the Cu-T users showed a significant decrease to 2.52 ± 0.17 mg. Cu-T induced also a decrease in the polysomes. The latter was complexes of the Ribosomes attached to one molecule of messenger RNA which is the functional unit active in protein biosynthesis. It was assumed that the decreasing amount of polysomes in the secretory endometrium reflected in impairment by the Cu of the normal protein synthetic processes.

Hicks and Cowchers (1975) postulated that the fucose and sialic acid concentrations of the endometrium were under endocrinological control and it had been postulated that the special polarity of the membrane was important during sperm capicitation and/or egg nidation.

Tatum (1977) observed increased content of copper in uterine fluid and also slightly in the myometrium in areas adjacent to copper device. Initially the increase was in both phases and later mainly in secretory phase.

Cu-T had specific effects on the secretory endometrium and these were related to a significant increase in Cu content in secretory as compared with proliferative endometrium.

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Other Enzymatic Alterations:

- Amylase - activity, which was normally more in secretory phase, than proliferative one, due to copper levels being depressed during both phases.

- Glycogen - synthetase, which was normally increased throughout, copper prevents this normal increase.

Oster (1972) reported that the chemical action of copper was the degradation of S-S contained protein, resulting in precipitation of albumin, inactivation of enzymes and decreased elasticity of uterine mucus.

It was suggested by Tatum (1973), that the copper reduces the rate of catabolism of glycogen.

In the study of Tamaya of Okanda (1976) in vitro, copper inhibited steriod hormone - receptor binding with Ki (inhibitor constant) = 2.7×10^{-5}M, to oestrogen receptors with Ki = 5.1×0.10^{-6}M to progesterone receptors - or Copper was more sensitive to progesterone receptor than to oestrogen. The sedimentation pattern demonstrated that copper aggregated or dissociated steriod hormone receptor macro molecules. These changes make receptors biologically inactive.

Morphologically, according to the same study, progestational proliferation was severely inhibited and estro-genicity seemed also to be inhibited. The greater stability of the oestrogen receptor would explain the increased estradiol uptake in the rat uteri with a Cu IUCDs in place. (Aedo and Zipper 1973).

Tamaya etal (1976) had noted stromal hypertrophy and decidua formation was inhibited in the rat and these effects were considered oestrogenic instead of the result of the inactivated progestational activity.

In recent years, Das, etal (1977) suggested that IUCD were acting through release of prostaglandins. The prostaglandins released could exert contraceptive action by various means, such as direct stimulation of uterine mobility causing premature expulsion of blastocyst (Bengtsson etal 1967). This according

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to Ducharme, etal (1968) was by means of its potent vaso-constriction activity, which led to congestion of the endometrium, impairing its ability to form decidua and leucocytic effect of Prostaglandin which was not confirmed in human beings as yet.

The data presented by Das, etal (1977) certainly showed a trend towards an increase in the rate of metabolism of Prostaglandin E due to IUCDs.

Utilising transmission and scanning electron microscopy Gonzalez Angulo etal (1976), further investigated epithelial, glandular and stromal changes possibly related to the copper effect. The observations indicated that there was a definite alteration of mito chondria of epithelial cells which resulted in impairment of respiratory mechanism and energy production, rendering the endometrial environment inhospitable to the fertilised egg.

Under experimental conditions copper had been found to be lethal to the mouse blastocyst by Brinster, etal (1974). This had been observed with human blastocyst also (inhibited the maintenance of blastocyst survival before implantation), by Nefnawi, etal (1975).

Nilsson, etal (1974) studied that indirect influence could be the iipaired degradation of glycogen, resulting in interference with the viability of blastocyst.

According to Nefnawi, etal (1975), released copper in the cervix had a direct lethal action on spermatozoa, altered enzymes essential of metabolism of sperm, changed the rheological properties of cervical mucus. However, these effects seemed to be less important than enzyme system interference.

Although the detected effects could explain some of the biological effects observed, they did not answer the question of why intrauterine copper or progesterone did not produce 100% inhibition of fertility.

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ORAL CONTRACEPTIVES:

The oral contraceptives prevent pregnancy by -

- Inhibiting ovulation.
- Increasing the viscosity of cervical mucus, thus forming a barrier to spermatozoa.
- Changing the rate of ovum transport through the oviducts.
- Making the endometrum less suitable for implantation.

The combination of steroid hormones in oral contraceptives act both centrally and peripherally to alter normal reproduction function.

Central Mechanism of Contraceptive Action:

According to Goldzieher, etal (1970) it had been known for many years that long term treatment with oral contraceptives not only caused an abolition of the mid-cycle surge of both FSH and LH but also suppressed basal levels of LH and FSH. The site of action where contraceptive steroids exerted most of their gonado tropin-inhibiting action had yet to be clearly defined.

Kastin, etal (1972) administered gonadotropin releasing hormone (GNRH) to females following short term use of oral contraceptives. They found a rise in FSH and LH that did not differ significantly from that of control subjects as the pituitary response to the hypothalamic GNRH was normal, these early studies suggested that contraceptive steroids suppressed gonadotropins at the level of the hypothalmus or higher in the central nervous system.

Kesseru-Kosa, etal (1973) and Rosenfield, (1974) claimed that Progestogens probably effect ovulation by acting on the hypothalamus pituitary axis, causing suppression of the surge of luteinizing hormone (LH) normally seen at mid-cycle just prior to ovulation. Without that surge ovulation does not take place.

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Other investigators, Perez-lopez etal (1975) and Mishell etal (1977), however reported that the administration of GnRH to women who had been ingesting oral contraceptives containing combinations of oestrogens and progestins for longer periods resulted in a significantly lower release of both LH and FSH, when compared with controls.

Effects on Pituitary

Apeflebaum and Taleisnik (1977) had found that the concentration of both LH and FSH within superfused rat hemi-pituitaries was increased in a dose dependent manner in response to oestradiol. In contrast, there was no acute effect of progesterone on pituitary cell content of FSH and LH indicating that progesterones stimulatory effect was due to change in pituitary sensitivity to GnRH rather than to de-novo synthesis of the gonadotropins.

Mishell, etal (1977) had provided evidence in humans that the combined use of oestrogens and progestins had a direct suppressive effect on pituitary gonadotropins in the majority of oral contraceptive users.

Nsenh and his colleagues (1979) had also documented an increased sensitivity of rat pituicytes in culture to GnRH following oestradiol exposure. In their study, progesterone alone did not affect the LH response to GnRH, but when given in combination with oestrogen, the sensitising effect of oestradiol was antagonised. In contrast to the study of Apeflebaum and Taleisnik, the intracellular content of LH was not affected by either estradiol or progesterone.

The extent of hypothalmic-pituitary suppression appeared to be dose related. Spellacy etal (1980) showed by sequential pituitary stimulation with GnRH that oral contraceptives 50 mg or more of ethinyl estradiol suppressed gonadotropin release to a greater extent than the lower dose formulations.

Peripherial effects of Oral Contraceptives

On Ovary

Johannisson, etal (1965) reported that the cyclical

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administration of progestin and oestrogen did not block the stimulating effects of human gonadotropins on the ovary of women.

On Cervix :

The cervical mucus is maximally penetrable to sperm during the late follicular phase, when serum oestradiol concentration is maximal. Zanartu and Navarro (1968); Archari, (1969), El Mahgoub and Karim, (1972), reported that during the luteal phase, and also during use of oral contraceptives, the cervical mucus became thick, cellular and impenetrable to sperm. Progesterone counteracted the stimulatory effect of oestrogens on penetrability of cervical mucus, and there was a marked dimunition in the number of sperms entering the cervix. Some sperm, if penetrated the cervical mucus, were unable to reach the uterine cavity or oviducts.

On Oviducts:

Sperm transport into the distal ampulla the site of fertilisation, was also dependent on the sex-steriods.

Circumstantial evidence had been presented by Chang, M.c.(1967) that the contraceptive progestins had a direct effect on capicitation of sperm in addition to their action on tubal transport of gametes. Fertilisation rates were impaired following oviductal insemination of progestin-treated rabbits despite the direct proximity of sperm with egg.

Norgestrel had also been found to inhibit invitro fertilisation of hamster eggs by hamster sperm (Swatkin, etal 1970).

On Endometrium :

According to Csmeli (1969) and Finn and Martin there was evidence that the decidua played a role in regulating trophoblast outgrowth. It would not be unreasonable to assume that the glandular atrophy and stromal decidulisation that occured following chronic exposure, to contraceptive steroids resulted in an endometrial enviornment hostile to implanation and further growth of the embryo.

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SIDE EFFECTS

The following side-effects described by the use of different IUCDs were:-

A. Blood loss with IUCDs.
B. Pelvic pain.
C. IUCDs and Pelvic inflammatory disease.
D. Displacement of an IUCD.

A. Blood loss with Intrauterine Devices:

Excessive menstrual blood loss associated with IUCDs is considered a serious side effect where problems of poverty ill-health and fertility contribute to the high incidence of anaemia in women in developing countries.

In a study from England, Morhead and colleagues (1975) found that IUCDs caused a mean Haemoglobin decrease of about 0.5 gm % in the first six months of use. However, Intrauterine cervical device rarely cause anaemia when there is adequate amount of iron in the diet.

Mainly three types of menstrual irregularity can occur with IUCD in situ:

- Increased volume of flow.
- Change of the timing and increased duration of blood-flow.
- Increase in intermenstrual spotting.

Leidholm etal (1975) reported that the mean increase in the menstrual blood loss after insertion of a Cu 'T' was 26 ml. an increase of 84% over the control cycle.

The smaller increase in bleeding with Cu IUCDs as compared with Lippes loop seemed to be caused by the smaller area of the device rather than the addition of copper. Hefnawi etal (1977) showed that addition of Cu to the Lippes loop produced even more bleeding during the first six months.

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Several studies, done by Malmquist etal (1974), Guillebaud etal (1978) in different countried have shown prolonged duration of flow in women using IUCDs. According to these studies, the duration was prolonged from 0.5 to 1.5 days for users of Cu IUCDs. In comparison to Lippes loop, the duration of flow is slightly more in Cu IUCDs.

There are several hypothesis to explain the reasons for these menstrual changes, which have been grouped under the following headings:-

1. Altered endometrial morphology.
2. Focata glanding and IUCD induced bleeding.
3. Activated endometrial fibrinolysis.
4. Role of Endometrial Mast cells.
5. Platelet uptake and turnover in the presence of IUCDs.

Shaw, etal (1979) studied 3 specific areas in the hysterectomy specimens from women using IUCDs.

- Endometrium depressed by direct contact with the device.
- Endometrium adjacent to the depressed site, and
- Endometrium from a remote site.

The depressed area was usually blanched and did not exhibit evidence of haemorrhage. Remote endometrium was usually healthy in appearance although occasionally it was congested and haemorrhagic. Most of the changes occured in the endometrium adjacent to the depressed site. It was usually oedematous, congested and haemorrhagic. The authors suggested that this area was responsible for the IUCD induced bleeding and that the increase in vascular permeability, the endothelial gaps and the lack of platelets and fibrin leads to interstitial oedema and haemorrhage which eventually escaped into the uterine cavity.

B. Pelvic Pain :

One of the most significant factors necessitating IUCD removal was pelvic pain, including insertional pain, intermenstrual cramps, often associated with spotting and bleeding and increased M dysmenorrhoea.

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Gerald Tzabough in 1978 had summarized the incidence of, as well as the reasons fro, pelvic pain in presence of IUCD.

Pain on insertion:

Endocervical pain, whether elicited by a sound, dilator or IUCD was described as a very sharp needle like pain.

Intrauterine pain, as when a sound or IUCD was placed in the endometrial cavity, was generally interpreted as a very severe midline menstrual cramp that may radiate to the umbilicus. This pain was usually followed within one to two minutes by a dull aching pain that may last several hours to several days.

Vagovagal responses had been seen occasionally with the insertion of an IUCD. They were manifested by a faintness bradycardia, (rarely tachycardia or cardiac arrythmia), nausea, diaphoresis and syncope. ECG changes have been also reported in 10% of patients with Cu T 200 (Tzabough, 1978).

The management of vaso-vagal responses consisted of leg-elevation or the Trendelenburg position and if relief was not obtained within 5 to 10 mts. atropine (0.4 mg) could be used I.V. with good results. Only very rarely removal of the device was indicated.

The general observation was that IUCD induced pelvic pain was maximum with non-medicated IUCDs, less with the smaller Cu IUCDs and minimal with progesterone releasing device. When evaluating the pain in the IUCD patients, one must be extremely careful to exclude other causes of pelvic pain such as tubal pregnancy, pelvic infection, adnexal accident, gastroenteritis and appendicitus, urinary tract infection, ureteral calculus etc.

Tatum, etal (1973, 1975) and Van Os etal (1978) gave results that increased pain, bleeding and removal rates were directly proportional to the size, shape, consistency and volume of the IUCD.

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c. IUCDs and Pelvic Inflammatory Diseases

Studies by Lippes (1963) and Tietze (1966) showed pelvic infection rates in IUCD users ranging from 0.6 to 3.5 percent per year.

Wright and Laemmle (1968) studied contraceptive methods in a low socio-economic group of post-partum women and found in a five fold increase in the acute salpingitis rate in IUCD users versus oral contraceptive users.

With trans fundal aerobic and anaerobic cultures of the uterine cavity, Mishell and Moyer (1969) demonstrated that, although bacteria were always introduced into the endometrial cavity at the time of insertion of a loop, host defence eradicated most of these bacteria within 24 hours and endometrial cultures 30 days after insertion were always sterile. They concluded therefore, that the occurrence of acute salpingitis more than one month after insertion of an IUCD was usually due to venereal infection and was unrelated to the IUCD itself.

Targum and Wright (1974) in a retrospective case - control study noted that 48 percent of women with a first episode of acute salpingitis were wearing IUCDs compared to 90 percent of controls. Eschenbach, etal in 1977 reported that the risk of acute salpingitis was 4.4 times higher in IUCD users than in non-users.

Both barrier methods and oral contraceptives reduce the risk of developing acute salpingitis.(Eschenbach etal 1977). Therefore, it was not known whether IUCDs increased the chance of developing acute PID compared to the use of no contraception.

According to Hager, etal (1979) the pelvic infection occuring in IUCD users could be caused by a variety of organisms, including aerobic and anaerobic bacteria, mycoplasma and chalmydia. Pelvic actinomycosis, formerly quite rare, had now been reported in a number of IUCD users by Hager etal (1979).

Acute pelvic inflammatory disease, occuring within

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6 weeks of IUCD insertion was associated significantly more often with PHCS (P0.01) as reported by Onsrud (1980).

D. Displacement of an IUCD and related complications:

Improper insertion and displacement of IUCD has been shown to result more often in perforation, expulsion, removals (for pain and bleeding) and pregnancy by Tatum (1975), Hasson etal. (1976), perlmutter, (1978).

Hasson, etal (1976) observed that when the IUCD length was equal to or exceeded the length of the endometrial cavity, high event rates occurred in all studied groups (pregnancy, expulsion or medical removals). If the difference between cavity and IUCD length increased, the event rate diminished, reaching a minimum in the group where difference was between 1.25 to 1.75 cms. Event rates increased once again when small IUCDs were placed in the disproportionately large endometrial cavities, defined as cavities longer than the IUCDs by 2 or more centimeters.

(i) Expulsion : Kamal etal, 1973 explained that dis-oriented or misplaced device and a dimensional disproportion can excite uterine irritation, which provoked myometrial contractions causing the expulsion.

(ii) Perforations: According to Mishell (1979), the perforation rates for the Copper-7 and Copper-T in a large multiclinical studies are almost in the same range of these for the loop 1:1000 insertion.

Tatum (1976) identified four variables that influence the risk of fundal perforations:-

(a) Size, shape and consistency of the device.
(b) Status and configuration of the Uterus.
(c) Insertion technique, and
(d) The skill and experience of the operator.

Cervical perforations were a result of downward displacement of the device. This could occur with any device with a vertical arm such as the T or 7 devices. It has been reported by Mishell (1979) to range from about 1:600 to 1:1000

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insertions. A small plastic ball was added to the tip of the 'T' stem to reduce (Tatum, 1975) the incidence. Tatum (1975) and Lippes (1978) described that copper devices elicit an intense tissue reaction leading to the formation of omental adhesions and should be removed immediately.

(iii) Pregnancy with IUCD : Perlmutter, 1978 observed that upon hysteroscopy with an IUCD in situ had shown downward dislocation and misplacement of the IUCD in 62 percent of patients in whom pregnancy occurred. The cause of failure could not be determined in the remaining patients.

When pregnancy takes place with an IUCD in place, implantation takes place away from the device itself, so that the device was always extra amniotic.

(a) Congenital anomalies:

To date, there was no evidence of an increased incidence of congenital anomalies in infants born with an IUCD in Utero (Michell, 1979). Tatum etal (1976) reported that conceptions occurring with a Cu-T in place, which progressed to a size which permitted adequate examination for anomalies, only one infant had a congenital anomaly (Fibroma of the Vocal Cords). Another interesting observation was that of Honoum (1980), who reported that the abortuses, obtained from women currently wearing the IUCDs were consistently free of detectable heteroploid correlated morphologic abnormalities, which occurred with the same frequency in prior IUCD users and non-users.

(b) Foetal Deaths:

In all studies of pregnancy with IUCD in situ, the incidence of foetal deaths was not significantly increased.

(c) Spontaneous abortions:

Lewit (1970) claimed that if a petient conceived with an IUCD in place and the IUCD was not removed, the incidence of spontaneous abortion was 55 percent, approximately three times greater than general incidence of abortions. Tatum etal (1976), reported that if after conception, the IUCD is spontaneously expelled or if the appendage was visible and

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the IUCD was removed by traction, the incidence of spontaneous abortion was reduced to almost half the above. However, a significant increase in the incidence of spontaneous abortion had been consistently observed by Mishell 1979.

(d) Septic abortions:

Tatum etal (1976) told that copper devices do cause septic abortions, although the indicence was not very high and could be further reduced by the early removal of the device.

(e) Premature Delivery:

The risk of premature delivery was 4 times higher in presence of IUCD versus early removal.(Tatum etal 1976).

(f) Ectopic pregnancy:

According to Mishell (1979), if a patient conceived with an IUCD in place her chances of having an ectopic pregnancy ranged from 3 percent to 9 percent. This incidence was about ten times greater than the reported ectopic pregnancy frequency of 0.3% to 0.7% of total births in similar population.

ORAL CONTRACEPTIVES

The following side effects were observed among users of oral contraceptives.

A. Nausea/Vomiting
B. Breakthrough Bleeding
C. Absence of withdrawal bleeding.
D. Depression
E. Weight Change.

Other Complications

F. Thrombiotic complications.
G. Myocardial Infarction.
H. Changes in Blood Pressure.

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I. Effect on the Liver.

J. Teratogenic Risks.

K. Carcinogenic Risk.

Inspite of having the highest theoritical effectiveness of the reversible methods of contraception, oral contraceptives have actual use failure rates no better than some barrier methods. In addition, discontinuation rates as high as 50-60% were seen in some family planning clinics as reported by Hatcher, etal (1980).

A. Nausea/Vomiting :

It was a common side effect associated with high-dose oestrogen therapy utilized in 'morning-after' contraception. Pill associated nausea usually occured early in the therapy and subsided as the therapy continued.

B. Break through Bleeding :

This is one of the most common pill-related side effect, occuring in almost half of the patients.

Two type of bleeding was identified -

- That which occured early during the initial months of use.
- and that which occured after several months of use.

The early bleeding resolved itself in 50% of the patients without treatment. It resulted from the inability of the synthetic hormones to stimulate and maintain the endometrium for the 3 weeks course of therapy.

The recommendation to determine at what time in the cycle, the bleeding occured in an attempt to determine the need for increased estrogen (early) or progesterone (late) was inability to predict the overall estrogen or progesterone potency of alternative pills to treat the bleeding. According to Speroff (1976), this increase in oestrogen dose should be a last resort, temporary if possible, and rarely will more than 4 50 mg pills be needed.

An important psychogenic effect also appeared to be

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present, for when women were informed of the possibility of menstrual irregularity, the frequency of breakthrough bleeding was increased.

Kanartu and Navarro (1968) noted that in 130 women uterine bleeding remained normal in 27, was decreased in amount or duration in 47, increased in 22, was very irregular in 24, and there was insufficient data in 10. The disturbance was usually tolerable.

Chinnatamby (1971) summarized her data by noting that there was complete disruption of the menstrual cycle with a totally unpredictable pattern of bleeding including amenorrhoea, hypermenorrhoea and spotting, which steadily diminished with time. Nine patients abadened therapy because of the spotting.

C. Absence of Withdrawal bleeding:

Because of the continuous progesterone administration, inhibiting the proliferative effect of estrogen on the endometrium, bleeding or withdrawal tends to diminish and in some patients may cease entirely.

Glimmer and associates (1978) have proposed another mechanism. They demonstrated that a less persistent suppression of the hypothalamus with the low dose pills resulted in FSH and estradiol production during the treatment free week. This endogenous estrogen production resulted in lack of withdrawal bleeding.

D. Depression :

Depression is reported to occur in approximately 5% of oral contraceptive users. Although some have suggested a psychological cause, there was also evidence by Wynn, etal (1975) that a disturbance in CNS neurotransmitters, particularly serotorin (5 hydoxy-tryptamine) was responsible.

E. Weight Change :

Patients taking oral contraceptives have been variously

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observed to -

1. Gain weight
2. Loose weight

and 3. Show no appreciable change in weight.

Hamecker,etal (1968) studied 104 patients and noted a mean gain of 5 pounds at 12 months and 10 pounds at 24 months more than 25 pounds, Rubio and Gonzalez (1970) in a study of 100 patients, found that 50 percent gained weight but at the rate of one and a half pounds a year.

Zartman (1970), reviewing 480 patients, reported an average gain of 4.8 pounds at 9 months and 5.7 pounds at 12 months. Mishell and associates (1968) found that 20% his 100 patients gained weight (mean 6 pounds). The overall gain per patient was 2 pounds in 12 months.

Seymour and Powell (1970) in their series of 732 patients fougd that 67 percent gained weight, 8% remained unchanged and 25 percent lost weight. The overall gain in 12 months was 9 pounds. Spellacy and colleagues (1970),(1972) noted an average gain of 5.5 pounds at 6 months in a group of 47 women.

Gladwyn Leiman (1972) in a study of 1507 patients found that 66% of the patients showed a gain, 8% remained unchanged and 26% lost weight. The mean gain was 4.4 pounds per patients. Over a 6 months period, weight gain was responsible for drop out in 1.7% of women in the collaborative study (Schwallie and Assenza, 1973).

Talwar, etal (1977) stated that an individuals body weight at initiation of therapy had been shown to influence the incidence of minor-side effects. Under weight patients experienced more nausea, vomiting breast-discomfort, uterine cramps and weight gain than over weight patients.

Other Complications

F. Thrombotic complications

The first to suspect a thrombogenic effect of the pill was Jordan 1961. British Medical Research Council conducted a large retrospective statistical investigation of the frequency

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of thrombosis and their relation to oral contraceptives. The results of that study confirmed an association between oral contraceptive and thrombotic disease as studied by Inman (1968) and Vessey, etal (1968, 1969).

Corroborative evidence was also produced by Sartwell, etal (1969). Stolley, etal (1975) and follow ups of the Britishi studies (Kay 1975 and Beral 1977). Yet retrospective studies by Drill and Calhoun (1972) and the well known prospective study from Puerto-Rico by Fuertes-de-la Haba and associates in 1973 failed to produce any such evidence. The relationship between the use of oral contraceptives and thrombiotic disease was still debatable as reviewed by Mougie (1973) and by Goldzeiher and Dozier (1975).

According to some authors, like Grant (1969), Inman etal (1970), McQueen (1970), it is the oestrogenic component of oral contraceptives that was responsible for the possibly thrombogenic effect of the pill.

Coagulation factors :

According to Nelsson, etal (1967) coagulation factors fibrinogen II, VII and X and factors VIII were increased in women using oral contraceptives.

G. Myocardial Infarctions

A casual relationship had long been suspected between the use of oral-contraceptives and myocardial infarction, especially in women for whom the risk of such infarction was increased for other reasons. This was studied by Inman (1970) Kuhik etal (1972) and Radford, etal (1973). In retrospective studies, Mann (1975) produced further evidence for such a relationship.

H. Change in Blood Pressure:

It was observed by Low and Oparil (1975) and Lund and Jensen (1975), that Benign Hypertension occurred in women who used oral contraceptives. Rarely, it was malignant. Zech, etal (1975) described a patient who developed malignant hypertension and irreversible renal failure during the use of oral contraceptives.

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Boyd etal (1975) reported intra renal degenerative changes in the vessels in a series of nine contraceptive users who also developed reversible hypertension.

In 1967 Laragh, etal associated hypertension with oral contraceptive use and proposed the following mechanism by which hypertension was induced. The rise in blood pressure induced by the pill had been explained as an effect on the renin-angiotension aldosterone system. Estrogens induced release from the liver of globulin substrate for renin i.e. angiotensinogens. Renin acts on these substrates to form angiotensins, which in turn act on the arterioles both directly and by inducing the release of catechol amines and aldosterone.

Hannecker and associates (1970) found no changes in diastolic blood pressure but commented that the systolic blood pressure tended to fall slightly conversely. Hartman (1970) indicated that in his 480 patients no changes in systolic blood pressure occurred and that the diastolic level tended to fall slightly.

It was interesting that the Royal College of General Practioners study on oral contraception (1974) demonstrated no relationship between oestrogen dosage and hypertension.

However, Pritchard and Pritchart (1977) showed that only 6 percent of women who were overtly hypertensive during pregnancy had significantly elevated blood pressures (with diastolic pressure greater than 90 mm) while taking the oral contraceptives.

I. <u>Effect on the liver:</u>

The changes in plasma proteins produced by the liver were related to the oestrogen dose according to Briggs and Briggs (1971).

Rannevik etal (1972) studied women who had previously had hepatosis during pregnancy regarding any effect of oral contraceptives of the liver. These changes were modified by norgestrel, but not by other progestogens again as stated by Briggs and Briggs (1971, 1976).

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Evidence of an increased frequency of gallbladder disease had been reported by the Boston - Collaborative Drug Surveillance Programme (1973) of 212 patients with gallbladder disease, 31 percent were oral contraceptive users, compared with 20 percent in 842 patients. Also in the British Prospective Study (1974) and reports of Stolley etal (1975) more gallbladder disease was more common among oral contraceptive users.

Cases of rupture of a liver adenoma and extra abdominal bleeding had also been reported due to oral contractives by Neumann and David (1973), Fredrick, etal (1974) and Antoniades and Brooks (1975).

A conceivable association between oral contraceptives and hepato cellular carcinomatas had been reported by Neuberger, etal (1980).

J. <u>Teratogenic risks</u>

According to Kaufman (1973), Nora and Nora (1973), Nora and Nora (1974), Janerich etal (1974), Nora and Nora (1975), the teratogenic risk is small, probably no greater than 7 per 10,000 births and probably occured in conjunction with some type of maternal predisposition (Nora and Nora 1974).

Nora, etal (1975) published a preliminary report of a prospective study of women who had taken combined oral contraceptives during their first pregnancy trimester.

Lauritsen (1975) found no difference in the frequency of chromosomal anomalies in abortions and oral contraceptive users, versus non-users. Thus there was no evidence that pregnancy after discontinuation of oral contraceptives involved any teratogenic risk.

Evaluating women who had discontinued the use of oral contraceptives before pregnancy, Doering, etal (1976) found no difference in the frequency of prematurity, perinatal mortality or congestive anomalies. The frequency of spontaneous abortions was 9.2 percent in the control group, compared with 8.6 percent in the group which had previously used oral contraceptives.

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In a large majority of 1448 infants whose mothers had stopped using oral contraceptives shortly before conception, Heuthman and Louik (1978) did not find any major teratogenic hazard.

K. Carcinogenic risk:

Original data from Cohort studies showed no association of the pill with breast cancer. The data from the Royal College of General Practioners study (1974) and the Walnut Creek Contraceptive study (1975) suggested slightly increased risk of breast cancer in women under 35 years of age with prolonged oral contraceptive use.

Vessey etal (1976) found no increased risk.

Oral contraceptives are said to reduce the frequency of breast tumours. In a large prospective study, Ory, etal (1976) following up 97254 women, 25-49 years of age. The rate of breast cancer was lower than among non-users of the pill, though the difference was not statistically significant.

On Endometrium

Vanderick etal (1975), examined 1348 endometrial biopsies of specimens from 748 patients using sequential pills, noted an increased frequency of cystic hyperplasia in 24.48% of the cases.

In 1975, Silverberg, Makowski and Lyon reported the occurance of endometrial carcinoma in young women who were taking sequential oral contraceptives.

According to Vessey, etal (1979) and Kaufman, etal (1980), their is any much evidence of an increased endometrial cancer in women using combined oral contraceptives.

CYTOLOGY

INTRAUTERINE DEVICES:

Health and disease were accurately reflected in cellular patterns. Cellular samples were like microbiopsies by which the cytopathologists, studied the multiple processes of health and disease to arrive at interpretations or diagnosis of conditions present. The cytology samples may be extremely small still at times they hold more information than large tissue samples removed by surgery.

Exfoliative cytology is the study of cells that were exfoliated from the surface of various epithelia (Kleinman, 1971). Although coming from the surface of organs, these samples reflected the deeper processes accurately. They covered a wider surface for examination than the biopsies could they afford unequalled opportunity not only to detect and diagnose disease but also to study the biologic behaviour of disease processes unaltered by surgical intervention or surgical removal (Frost, 1974).

Clinical Cytopathology was first successfully introduced by Papanicolaou and Traut in 1943. Papanicolaou's technique had come to be widely accepted as a diagnostic tool for early cancer in various organs of the body.

Professor, Dr. Rudolf Virchow, the father of 'Cellular Pathology' had left the famous saying, 'Omnis Cellulae cellula". Even a single cancer cell can be biologically malignant and this smallest unit may possess the distinctive features that fulfill the criteria of malignancy. Takahashi, etal (1971) stated that precise recognition of cellular alterations was the basis of exfoliative cytology.

Jeffcoate (1975) described that the secretions lying in the upper vagina normally contained cells desquamated from the vaginal wall, the vaginal aspect of the cervix, the endo-cervix, the endometrium and sometimes the tubes. The examination of material in the vaginal pool was first suggested and used by Papanicolaou.

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The vagina and the portio-vaginalis of the cervix are covered by stratified squamous epithelium. There are five layers or zones of cells according to the original description of Dierke's (1927), to his histilogical explanation was added the cytological appearance described by Grubb(1977).

Histological :

(1) The lower most portion, formed by basal or germinal cells, cells from these layers do not exfoliate.

(2) Several layers of polyhedral cells with large nuclei and prominent intercellular bridges (prickle cells parabasal cells, spinal cells or stratum spinosum profundum).

(3) Clear light zone (intermediate zone, navicular zone or stratum spinosum superficial) cells are large, moderately flat, highly vacuolated, with vesicular nuclei, high glycogen content and variable number of granular inclusions.

(4) This layer was variable, best seen in presence of Keratinization, as following oestrogen therapy or with prolapse. It is a narrow band of deeply stained flattened cells, which contained Keratohyaline granules, zone of cornification or condensation (middle zone, intermediate zone or stratum granulosum).

(5) Superficial layer or stratum corneum- elongated, flattened cells with small Pyknotic nuclei.

Cells of all these layers except the first were seen in the vaginal smears.

Intrauterine Devices and Carcinogenesis:

Carcinogenic potential of the intrauterine devices was one of the controversial points.

Unmedicated Devices:

Oppenheimer, etal (1948) and Southam and coworkers (1966), had clearly established the oncogenic potential of plastics embedded subcutaneously.

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Cervical neoplasia maydevelop at varying periods in women using Lippes Loop as described by Mazgulies (1964), Tietze (1966) and Tichauer, etal (1968).

Ishihama and Nagabu (1964) in combined histo-cytological study, Arya (1965) in cytological study had reported only a few instances of dysplasia in women, using different intra-uterine devices for varying periods.

In 1966 World Health Organisation (WHO) Scientific group reported that histological studies on uteri of many hundreds of women, wearing intrauterine devices had failed to reveal any changes related to neoplasia.

Corfman and Richart (1967) observed epidermoid carcino-mata in the rat uterus following a prolonged exposure to polyethylene and stainless steel devices.

Richart and Barron (1967), analysed the progression of cervical dysplasia to carcinoma in situ in women having Intrauterine devices and failed to find a significant difference from the control group.

Cytological studies of Schwartz, etal (1967), Sagizoglu, etal (1970), had also failed to detect any evidence of precancerous or malignant changes in the cervical epithelium of women, retaining an intrauterine device for as long as six years. The reported incidence of dysplasia was found almost identical to that in control. Most of the dysplasia showed regression to normal at their follow up six to twelve months later.

Ishihama etal (1970) again in a cytological study in women using intrauterine devices reported suspicious smears in 68 (6.4%) out of 1058 women. But they had not reported any malignant changes in final histopathological diagnosis among these 68 women.

Medicated Devices

Retrospective and prospective studies had failed to suggest any carcinogenic action of Copper upon the genetive tract. Tatum (1972) studied serial Papanicolaou smears of the

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cervical epithelium. These he found to be normal over a period of use Copper 'T' for as long as 5 years.

In 1974, Tatum, reported that repitative endometrial biopsies from women who had worn a copper bearing T for 5 years showed no greater incidence of endometrial hyperplasia or malignancy.

Dysplasia, Inflammation and Infection with Intrauterine Contraceptive Devices:

Affandi and Vithar (1976) followed 200 women, who used copper device for contraception, by cytological smear examination. The study was conducted for a period of 4 years They reported 5 smears of mild and 3 smears of moderate dysplasia. Cases with dysplasia showed a regression to normal in the follow up smears in a period of one to two years after treatment.

There had been some reports of infection in women using Intrauterine Devices. This infection warranted the removal of the device.

All patients who showed inflamation were promptly relieved by treatment.

Cytomorphological analysis of 2135 women, who used Copper-Intrauterine Contraceptive Devices for 24 months had been reported from Indian by Luthra etal, (1977). The study did not show any significant cytomorphological abnormalities in relation to the period of use of Copper - Intrauterine Contraceptive Device. The data revealed the rate of cervical dysplasia among women who had initial negative or inflammatory smear to vary between 1.1 to 2.9% during 24 months of follow up. Although these cases had developed dysplasia during the use of Copper Intrauterine Devices, the rate was not significantly enhanced in comparison to that of the observed rate of cervical dysplasia in population of Delhi Urban area which was 2.6%. It has been observed again that the frequency of dysplastic lesions was higher at 6 and 12 months of follow up than during later months. It appeared that those women who were initially diagnosed as inflammatory had a slightly higher risk to progress into dysplastic lesions as compared

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to women with initially negative smears. Majority of the dysplastic lesions detected, showed regression during the period of follow-up. Although in one case initially severe dysplasia was found, which progressed to carcinoma in situ, within 2 months of flocw-up, this could not be related to the use of Copper-Intrauterine Contraceptive Device as the period of use was too short for any reasonable conclusion. Opinions varied regarding the latent period required to develop Carcinoma from dysplastic lesions. A number of prospective studies by Richart and Barron (1969) and Gellman (1976) suggested that 1 to 30 years period was needed for a dysplasia to progress into carcinoma.

Another interesting point in the study of Luthra, etal (1977), was the observation that a sizable portion of dysplastic lesions showed healthy cervix on pelvic examination. It appeared that cytopathological changes preceded the clinical manifestation. The cervical examination could detect the cervical abnormalities even though the clinical examination failed to detect the abnormalities at the early stage. This signified the importance of regular cytological examination in women who used contraceptives on a long term basis.

Misra, etal (1977) carried out comparitive cytological studies in 110 women using Lippe loop and 90 women with Cu-Intrauterine Contraceptive Devices for a period ranging from 3 to 5 years. No case of several dysplasia or malignancy was found in either group on follow up. The incidence of dysplasia was slightly higher in Cu-T users than in loop users. The incidence of inflammation was also higher in the Cu-T group. This was related to the release of copper by the device as suggested by Hagenfeldt and this hypothesis was supported by the fact that the percentage of inflammatory smears tended to decline with prolonged use of the device as the release of copper diminished. In the smears showing inflammation Trichomonas vaginalis was also present in a few patients. This too was cured by treatment.

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Luthra, etal (1980) had reported their experience with the use of Cu-devices for 48 months. 30 women had dysplasia in the smears initially before insertion and equal numbers developed dysplasia during the follow up. At the end of 48 months all the dysplastic changes regressed to normal. It had been revealed the lesser the severity of the dysplastic lesion, greater was the likelihood of regression. (Luthra, etal 1969).

Aikat and colleagues (1980) reported the results of long-term effects of Cu-Intrauterine contraceptive devices on cervical epithelium and endometrium. Eight hundred thirty three women, who were using various Cu-IUCDs were studied. There was mild dysplasia in 3 and moderate in 2 prior to insertion. However, some regressed within 6 months of follow up. Dysplasia (all mild) which occurred during follow up also regressed within 6 to 12 months. The study of 91 endometria with Cu-Intrauterine contraceptive devices for 1 to 6-1/2 years, showed endometritis in 6 patients and hormonal imbalance in 17 cases. To compare them with those cases who had loop inserted, the incidence of inflammation was higher. It was concluded that Copper-IUCDs on prolonged use produced neither dysplasia nor malignancy in the cervical epithelium or in the endometrium.

It was evident that only long term cytological study could supply useful information. The lack of such study for Cu-IUCDs, perhaps was due to restricted life of the previous available Cu-Intrauterine contraceptive Devices.

INFLUENCE OF ORALS ON VAGINAL EPITHELIUM SEEN IN CYTOLOGY:

After administration of hormonal contraceptives, the vaginal cell pattern did not resemble to that of the normal corpus luteum phase nor that of an early pregnancy. The cytology rather showed a progesterone effect with decreased oestrogenic influence. The histological structure of vaginal epithelium corresponded to the cytologic patterns.

While millions of women all over the world had been

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using steroidal compounds for contraception during the last decade, a great concern had risen over the potential carcinogenic effect of these compounds on the reproductive tract.

Reports on this subject were contradictory with oral contraceptives certain workers had found no increase in the incidence of squamous dysplasia or carcinoma in situ of cervix, while others had found highly significant correlations between the use of oral contraceptives and occurance of cervical dysplasia.

Orals and Carcinogenesis:

Ayre etal, (1966), studied 782 women during or after cyclic continous Enovid medication. The conclusion was Enovid showed no indications of carcinogenic influence even in pre-existing, pre-malignant dysplasia or carcinoma in situ of the cervix.

Weid, etal (1966) found no significant atypical changes in the examination of female genital tract smears from 1,620 patients taking contraceptive hormones.

Secost (1968) in order to classify the possible cancerous effects of ovulation inhibitors carried out cytologic and colposcopic examinations on 1,031 women who had taken ovulation inhibitors during 9,771 cycles. The histologically proven cervical carcinomas and epithetial atypias were found to be 0.44% which was about the same percentage as found in routine examinations of healthy women in the mass screening programme conducted by Erickson etal (1956) who found 0.7% invasive and carcinoma in situ in women of all age groups.

Ayre etal (1966) in their study on 1020 women reported some degree of regression of cellular lesions by the use of oral contraceptive.

Boyce,etal (1972) studied 196 consecutive patients with cervical carcinoma, prospectively. The study was designed to determine whether patients with cervical carcinoma used oral contraceptives to a growth extent than did control subjects.

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Their data did not confirm an increase in cervical carcinoma among women who used hormonal contraceptives. Miller (1973) matched oral contraceptive users (2,394) from a Connecticut (USA) town with non-users of same age (within 2 years otherwise chosen at random from 16,175 non-user residents of the same town. Remarkable similarities in cytology between the test and control group oef each age bracket was found.

So rates of cervical neoplasia were lower for users or oral contraceptives, than controls in two studies - Tyler (1964), Pincus, etal (1965), no different in four studies (Naque, etal 1965, Weid etal 1966, Worth etal 1972). No association was found between the use of oral contraceptives and cervical neoplasia (Roy Choudhary, 1980).

Dysplasia and infection with orals:

Attwood (1966) stated that among 500 medicated women there was a 22% incidence of dysplasia where as among 9000 controls there way only a 0.8% incidence.

However, Guhr, (1966) emphasised that ovulation inhibitors induced changes in the squamous epithelium of the portio-vaginalis of every case ranging from early parakeratatic cornification to findings suggestive of carcinoma.

Liu, etal (1967) noted 18 abnormal smears from 1000 women (18% incidence) treated with hormones for contraception. That is they showed an enlarged nuclei hyperchromatism and nuclear abnormalities.

Melamid,etal (1969) revealed an increase in the prevalence of severe dysplasia and in situ carcinoma in oral steroid users. They studied 27,500 women who had chosed to use oral steroids for contraception and 6,809 women who chose diaphragm. Prevalene rate of cervical cancer was 14 per 1000 in oral steroid users and 4.3 per 1000 in diaphragm users.

Kline, etal (1970) in their study on 2,296 women on contraceptive therapy, 2% had atypical cells as in ~~contrast~~ to 17,724 women (controls) in whom incidence was 1%.

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El Mahgoub and Karim (1972) in their study on 171 women on the long-term use of injectable contraceptives did not find any criterion suggestive or conclusive of negligency.

In the study by Wallach, etal (1970) in 385 patients, they noticed cervical dysplasia in 11 patients and dysplasia with focal carcinoma in situ in one patient.

Maguso, etal (1966) reported on 43 women receiving high levels of oral progestational compounds with little or no oestrogen observed that 14% had endocervical hyperplasia.

Taylor, etal (1967) found atypical polypoid endocervical hyperplasia in 13 patients all taking progestin like agents for contraception.

Candy and Abell (1968) described similar lesions in 15 patients, they also noted a few atypical parabasal cells, as well as columnar cell atypia, in 13 of the patients for whom cytologic material was available.

Chiaffitelli and Domingue, (1970) conducted a survey using sequential or rhythmic and combined oral contraceptives. In patients on sequential therapy, a rushed increase of oestrogenic action was observed. This was probably due to medicinal accumulation. The moderate effect of the stimulation of different progestogens coincided with the observations of other authors. Weid (1958) found that the effect of different progestogens on highly proliferative epithelium due to previous oestrogen stimulation was shown by a second phase with more mature types than usual. The cellular folding in the first phase of the last cycles of treatment coincided with Pundel's statement (1968), that when oestrogens were administered in high doses and for a long period of time the superficial cells, flat at the begining started to fold.

In patients on combined oral steroids no cyclic variation was observed. There was a progressive increase of intermediate type of desquamation, as treatment continued.

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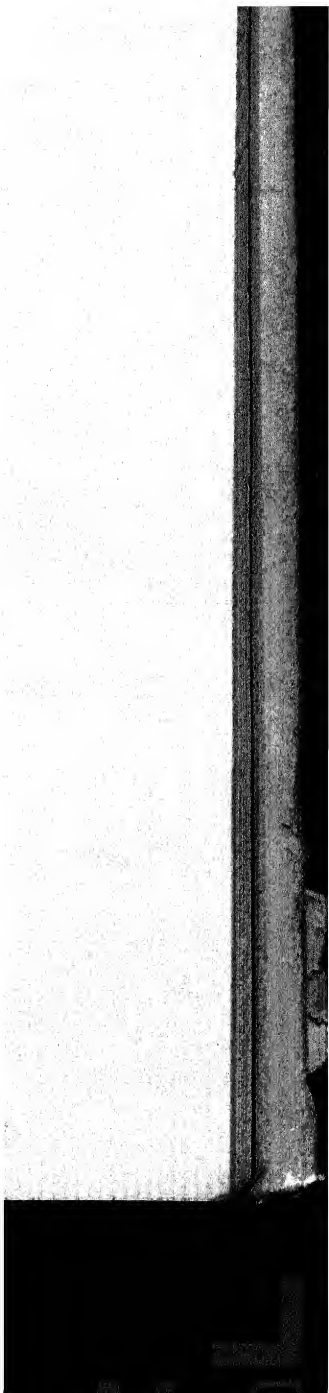
The predominance of intermediate type desquamation co-incided with that observed by Perrin (1964), Schockaert (1964), Jackson (1964), and Rice-Wray (1965), who all performed investigations on a similar therapy regimen. Cytolytic patterns mentioned by Jackson and Linn (1964) referred to the absence of the superficial layer of the epithelium, and were related to the appearance of androgenic action in traces.

It had been hypothetised that continous progestrogen contraception would be more likely to stimulate carcinogenesis than cyclical combined oestrogen-progestrogen contraception because an unchanged hormonal enviornment encouraged mutant cells to multiply unchecked, whereas a changing hormonal enviornment could check this growth. (Ravenhold 1972). This had not been proved, however.

MATERIAL AND METHODS



MATERIAL AND METHODS

The present study was carried out in the Department of Obstetrics and Gynaecology and in the Department of Pathology at M.L.B.Medical College and Hospital, Jhansi in a study period from 1 May 1982 to 30 April, 1983.

(A) Selection of Cases :

Cases for the present study were selected from Post-partum,Deptt. of Obstetrics and Gynaecology from Gynaecological out patient department and indoor wards of the Department of Obstetrics and Gynaecology.

This study comprises of 292 cases. The cases studied are divided into two Groups.

I. Study Group:

(i) Postnatal cases.
(ii) Cases after medical termination of pregnancy.
(iii) General patients willing to adopt temporary methods for spacing.
(iv) Patients already using the temporary methods of contraception.

II. Control Group:

The Control Group comprises of patients of same age and parity. But these patients are not using any contraceptive device, at present, neither have they used it in the past.

(B) Clinical study -

All the cases were further evaluated under following headings.

I. Age Group -

All the patients were in the age group of 19 years to 40 years with a parity of 1 to 6 children.

II. History -

History included complete interrogation of the

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patient, a full account of the menstrual history with details about catamania, last menstrual period, any withdrawal bleeding or break through bleeding. Also full details of obstetrical history including the number of alive children and last child birth. Any history of abortions or still births is also noted.

XII. Enquiry in detail regarding changes after use:

(i) Check up after use of contraceptive method.
(ii) About menstrual irregularities or withdrawal bleeding.
(iii) About effect on subsequent fertility.
(iv) Pain or any vaginal discharge.
(v) History of expulsion of IUCD or missing the oral pills.
(vi) Time and reason, if device is discontinued.

XV. Examination of the patient :

(i) General examination :

A through general examination was done with special attension as regards to pallour, oedema, blood-pressure and weight of the patient.

(ii) Systemic examination :-

Brief systemic examination of Cardio-vascular system, respiratory system, central nervous system and of Gastro-intestinal system was done. This was just to exclude any systemic disease because some of them may be responsible for the withdrawal of the device or for several other side-effect.

(iii) Local examination :

In this a perspeculum, per vaginum and bimanual examination was done.

(a) Perspeculum examination :

It was done to inspect the cervix and vaginal wall for any local pathology.

(b) Per Vaginum examination:

The vagina was examined by palpation. The

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direction and texture of cervix was determined.

(c) Bimanual examination :

The uterus and its appendages were examined bimanually to determine the position and size of the uterus. The ovaries were examined to determine any enlargement. The absence or presence of device in situ was also confirmed by this.

(C) Choice of Contraceptives:

(i) Condom.

(ii) IUCD - Lippes Loop
- Copper T 200

(iii) Oral contraceptives.

MATERIAL REQUIRED :

(i) Wooden spatula :

Used for taking the smears.

(ii) Glass-slides:

The glass slides used in the present study were of thin variety and cleaned and dried thoroughly before use. They were labelled in serial numbers by diamond pencil (glass-cutting pencil) and kept in a slide box.

(iii) Coplin Jars:

These were filled 3/4th with fixative (equal parts of 95 percent alcohol and ether). Each jar is a small jar which is divided in four chambers by a partial, glass partition.

(iv) Papanicolaou's staint

This is the stain used for staining the smears.

Preparation of Smears:

Collection of Smear and Fixation :

- Smear was taken before doing any gynaecological examination.
- Patient was put in lithotomy position.

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- Sim's speculum was applied after retracting Labia majora with left hand.
- The introitus thus widely opened was gently stroked with the spatula over the upper mediolateral vaginal wall.

The spatula should not touch the vulva or the cervical area in order to prevent contamination by erythrocytes. Vaginal cells are transferred from the lip of the spatula to the clear surface of the numbered slide. The material was then spread evenly on the slides without rubbing.

The slide was immediately dipped in coplin jars containing ether and alcohol.

Precautions:

1. Spatula must be clean and dry.
2. Smears should be made out in thin layers for thick smears do not stain uniformly.
3. The glass slides must be perfectly dry and clean.
4. Smears should be Be kept in coplin jars before any drying takes place.
5. The bottles of fixative should be kept away from the flame.

Fixation :

The time of fixation is atleast 15 minutes but not longer than 10 days.

Staining and Mounting of the Smears:

The fixed smears were processed and stained according to papanicolaou staining method. (H.Smelka and H.J.Geest, 1965) Technique was as follows-

The smear was dipped in-

80 percent alcohol	for half minute.
70 percent alcohol	for half minute.
50 percent alcohol	for half minute.
Distilled water	for half minute.
Harris Haematoxylin	for three minutes.

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Distilled water	for half minute	
25 percent aqueous hydrochloride acid	6 dips	
Running water	for six minutes	
Distilled water	for half minute	
Rinse in 50 percent alcohol		
Rinse in 70 percent alcohol		
Rinse in 80 percent alcohol		
Rinse in 95 percent alcohol		
Orange G-6 for two minutes		
95 percent alcohol	half minute	) Separate
95 percent alcohol	half minute	) Containers
EA 50 for one and half minute (Eosin Azure)		
95 percent alcohol for half minute		
95 percent alcohol for half minute		Separate
95 percent alcohol for half minute		containers
Absolute alcohol for half minute		
Xylol alcohol (in equal parts for half minute)		
Mount in D.P.X.		

Papanicolaou recommends that in order to prepare a 0.5 percent alcoholic solution of the stain, a 10 percent aqueous solution is first prepared to secure better solution and 95 percent of absolute alcohol would produce 0.5 percent solution in 95 percent alcohol. The solutions are filtered separately just prior to the final mixing.

Orange G-6 :

Orange G, 0.5 percent solution in 95 percent alcohol, 100.00 ml.

Phosphotungstic 0.015 gm.

Reading and Interpreting the cells smears:

Since the cellular spread was widely distributed on the slide the area to be studied was randomly selected. With the use of bloodcell calculators 100 cells were counted based on morphological appearance and staining character. The different vaginal cells are shown in Fig. 3.

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Superficial Cells:

These are large, delicate, polyhedral cells with sharply defined cell borders. Cytoplasm is light, transparent without structure and may be eosinophilic or basophilic. Nucleus is pyknotic.

Intermediate cells:

Are medium sized with extreme variation in size. Cytoplasm in most of the cells is basophilic. The nuclei are large and vesicular.

Parabasal cells:

Rounded cells with basophilic stain, Nucleus is large rounded with distinct structure.

Vaginal cytology was taken to detect the maturation index (M.I.)

Any Pelvic Infection
Inflamation
Dysplasia of mild, moderate or severe grade.

Maturation-Index :

The cyto hormonal evaluation expresses the level of cellular maturation attained at the time of exfoliation.

It is differential count of these major cell type shed from the stratified squamous epithelium and represents the relation of parabasal cells to Intermediate cells to superficial cells.

A differential count of superficial cells, intermediate cells and parabasal cells was performed. A count of two hundred cells has been made in differential fields and number of these cells were recorded. This was expressed following way for hundred cells as.

Maturation index = Parabasla cells/Intermediate cells/
Superficial cells

M.I. = P/I/S.

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Inflammation:

The smears with inflammatory changes showed collection of leucocytes often masking the epithelial cells and leucocytic inclusions in epithelial cells. In some cases polymorphs and Red blood cells are seen while in others collection of histocytes with presence of excessive mucus and occasional foreign body type of giant cells were seen.

Dysplasia:

Atypical cellular activity in an epithetial lesion is reflected in the exfoliated cell. It frequently appears as abnormal nuclear changes (dyskaryosis) or alteration in cytoplasmic maturation (i.e. dyskeratosis, immaturity) or both.

The Dyskaryotic cell

Papanicolaou characterized a group of cellular abnormalities involving mainly the nucleus, and called them dyskaryotic cells as a group.

The round or oval nucleus of the dyskaryotic is large and hyperchromatic. Its nuclear envelop is wavy or undulated not wrinkled or shrunken. The chromatin is minimally to coarsely granular, but is fairly evenly distributed throughout the nucleus.

Diagnostic changes in the cytoplasm of dyskaryotic cell involve mainly its ability to mature normally hypermaturity or dyskeratosis. Conversely immaturity brings inability to either squamify or produce columnar forms, and a decrease in the amount of cytoplasm both absolute and relative to the nucleus (increased nucleo-cytoplasmic ration).

Dysplasia can be graded into three grades, mild, moderate and severe, according to following criteria:

Mild Dysplasia (Grade I)

In ectocervical cells cellular abnormalities were mainly in Intermediate cells and superficial cells. Exfoliated cells were mostly single and showed cellular and nuclear

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enlargement without alteration of nucleocytoplasmic ratio. Cytoplasmic changes in the form of fine or large vacuoles and granulations were a prominent feature. Some precociously cornified parabasal cells were also present.

Moderate Dysplasia (Grade II):

The parabasis and Intermediate cells revealed more advanced cellular changes than were evident in superficial cells. The cells were exfoliated, single or in small groups and occasionly in syncitial masses. In groups small polarity was maintained. Cellular and nuclear enlargement with slightly increased nucleo-cytoplasmic ratio was observed. Cytoplasmic changes were similar to mild dysplasia.

Marked Dysplasia (Grade III):

The superficial as well as parabasal cells and intermediate cells were involved. The cells were exfoliated single in groups or in syncitial masses and showed loss of polarity in groups. Nucleocytoplasmic ratio was increased. Hyperchromasia, thickened nuclear membrane and prominent nucleoli were observed. Chromatin usually presented coarse granular pattern but was translucent in some. Abnormal squamoid forms like spindle cells, or tadpole cells were present.

Hanging Drop Preparation : For Trichomonas Vaginalis

A drop of vaginal secretion is taken on the coverslip It is mixed with normal saline (one drop). The cover slip is placed on a plasticin ring on a glass slide. This is examined under the microscope for presence of Trichomonas vaginalis.

Trichomonas vaginalis is a small univellular flagellated protozoon. It varies in size from 10-30 microns, usually stains grey-blue and contains multiplar red, intracytoplasmic granules. The small ovoid and vesicular nucleus must be identified for a definitive pear-shaped, but variations in its shape due to the arte facts are frequently encountered.

Endometrial Biopsy :

Instruments used

1. Sponge holding forceps.
2. Sim's speculum.

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3. Anteior vaginal wall retractor.
4. Volsellum.
5. Uterive sound.
6. Endometrial biopsy curette.

Preservative for biopsy materialst

Formalin.

Stain : Haematoxylin and eosin

Methodt

Patient is put in litholoury position.

Part was painted with sponge holding forceps.

Binanual examination was done to ascertain, the position of the uterus, and to exclude any pathology of the uterine adeneza.

Sim's speculum was inserted and the cervix was visulised with the help of anterior vaginal wall retractor.

Anterior lip of cervix was caught with volsellum.

Uterine sound was passed to know the length of the uterine cavity.

Endometrial tissue was taken out with the help of endometrail biopsy curette, and was fixed in 40 percent solution of formalsaline. This fixed tissue was processed in autotechnidon.

Sections were cut with the help of microtome 5 microns thickness.

Staining was done by routine haematoxylin, Eosin stain (D.P.X. culling. Histopathological techniques second edition 1963. 204).

Mounting was done in D.P.X.

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OBSERVATIONS

OBSERVATIONS

In the present study clinical and vaginal cytological changes were studied before and following the use of different contraceptives namely -

- Intrauterine contraceptive devices including :
  Copper 'T' and Lippes loop
- Oral Contraceptives
- Women with opposite condom users partners.

SELECTION OF CASES :

All the patients studied were divided into 2 groups -
(A) STUDY GROUP comprising of 252 cases.
(B) CONTROL GROUP comprising of 40 cases.

(A) STUDY GROUP :

Postnatal cases, cases after medical termination of pregnancy usually with a parity of more than 2 children and falling between the age-group of 20 years to 35 years, willing to adopt temporary methods of contraception were included in this study. Those patients, who were already using the above mentioned contraceptives devices were also included in the study group.

In all, there were 252 patients in the study group. A clinical, vaginal cytological and Endometrial histopathological follow up of allthese patients was done at 3 months and 9 months interval, before and following the use of different methods of contraceptives.

(B) CONTROL GROUP :

This group consisted of 40 patients, having the same parity and were of the same age group, as of the selection group. But these women were not using any contraceptive device.

A clinical, vaginal cytological and Endometrial histopathological examination of these patients was also performed according to the patients of Selection Group.

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Table XI : (Fig. 3) Showing the distribution of women according to the type of contraceptive used.

Type of contraceptive	Number of cases
Control Group	40
Copper 'T' users	152
Loop users	20
Users of oral contraceptives	50
Women having the opposite condom user partner	30
Total	292

Table XI shows the distribution of patients according to the device chosen i.e. 152 cases were copper 'T' users, 20 women were using Loop, 50 were on oral contraceptives and 30 women had an opposite condom user partner.

(1) Age :

Table XII : (Fig. 8)
: Showing distribution of women using different contraceptives according to age.

Age in years	Copper 'T' users		Loop Users		Users of oral contraceptive		Women with a condom user partner		Control group	
	Number	%	Number	%	Number	%	Number	%	Number	%
Below 20 years	6	(3.94)	-		-		-		-	
20-24 "	40	(26.31)	8	(40)	14	(28)	6	(20)	6	(15)
25-29 "	54	(35.52)	4	(20)	18	(36)	12	(40)	18	(45)
30-34 "	40	(26.31)	4	(20)	14	(28)	7	(23.33)	8	(20)
35-39 "	8	(5.26)	-		4	(8)	4	(13.33)	6	(15)
40 and above	4	(2.63)	4	(20)	-		1	(3.33)	2	(5)
	152		20		50		30		40	

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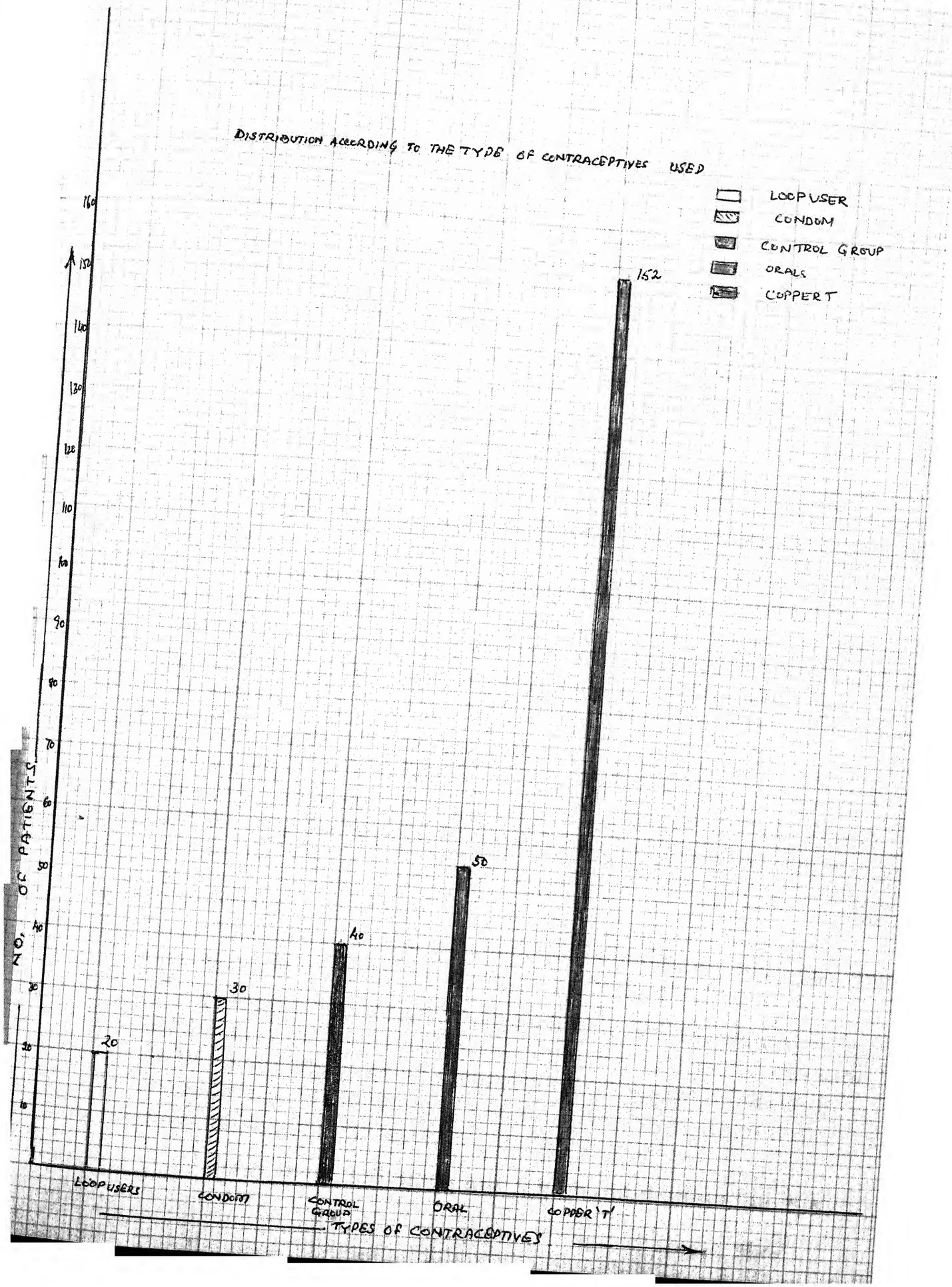
FIG 3


DISTRIBUTION ACCORDING TO THE TYPE OF CONTRACEPTIVES USED
LOOP USER
CONDOM
CONTROL GROUP
ORALS
COPPER T
NO. OF PATIENTS
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
20
30
40
50
152
LOOP USERS
CONDOM
CONTROL GROUP
ORAL
COPPER T
TYPES OF CONTRACEPTIVES

The distribution of women using different contraceptives according to age is shown in Table III.

Majority of the women (38.14%) using the Copper 'T' belonged in the age range of 20 years to 34 years. Maximum percentage (35.52%) were using the Copper 'T' the age of 25-29 years. Equal number (26.31%) were using the device between 20-24 years and 30-34 years. (3.94%) women used the device below 20 years and 2.63% used it above 40 years.

40% were seen using the loop at the age range of 20-24 years. Equal no. of women (20%) used this device in the age range of 25-29 years, 30-34 years and above 40 years.

Maximum number (36%) of women using oral contraceptives were present in the age group of 25-29 years. Equal number (20%) of women used this device at 20-24 years and 30-34 years. Only 8% cases were present between the age range of 35-39 years.

40% women had an opposite 'Condom user partner' at the range of 25-29 years. 23.33% women were present in the age of 30-34 years. 20% women were of 20-24 years and 13.33% were of 35-39 years range. Only 1 women (3.33%) was above 40 years.

Control Group : There were 40 women in the control group. 45% of women were of the age range of 25-29 years. 30% were of 30-39 years and 15% were of the age range of 20-24 years and 35-39 years range. Only 5% women were above the age of 40 years.

(2) PARITY :

The distribution of women using different contraceptives according to 'Parity' is shown in Table IV (Fig 6).

Copper 'T' users - Maximum number (37.5%) copper 'T' users had 3 children and 26.31% had a 4 children. 16.44% were having 2 children. Equal number 5.26% of women possessed 5 and more than 5 children. 2 women (1.31%) were Nulliparous among the copper 'T' users.

Loop users - 6 women had 3 sibs and 4 women had 2,4

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and more than 5 kids among the loop users.

Oral contraceptive users - Maximum number 40% of women using oral contraceptives had only 2 children, 20% were with only 1 child, 24% had 3 children and only 8% were with a parity of 4 issues.

Table XV : (Fig 8)
: Showing distribution of women using different contraceptive according to Parity)

Parity	Copper 'T' users	Loop users	Users of oral contraceptives	Women with condom user partner	Control group
Nulliparous	2 (1.31%)	-	-	-	-
1	12 (7.89%)	-	14 (28%)	7 (23.33%)	4 (10%)
2	25(16.44%)	4 (20%)	20 (40%)	14 (46.66%)	16 (40%)
3	57(37.50%)	8 (40%)	12 (24%)	4 (16.66%)	10 (25%)
4	40(26.31%)	4 (20%)	4 (8%)	2 (6.66%)	6 (15%)
5	8(5.26%)	-	-	2 (6.66%)	2 (5%)
Above 5	8(5.26%)	4 (20%)	-	-	2 (5%)
	152	20	50	30	40

Women with condom user partner - Maximum number (46.66%) of women had a parity of 2. (23.33%) women had only one child and 16.66% had 3 sibs. Equal number of women 6.66% were having a parity of 4 and 5.

Control Group :-

These women were not using any contraceptive in the present study nor previously. 40% had 2 children, 25% had 3 issues. 15% had 4 and 5% had 5 and more than 5 children. There was no nulliparous women in the control group.

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3. CLINICAL SIDE EFFECTS :

Table V : (Fig. 4)

: Showing incidence of various clinical side-effects in women using different contraceptives

Name of complication	Copper 'T' users		Loop Users		Oral Contraceptives users		Women with opposite condom partner	
	Number	%	Number	%	Number	%	Number	%
1. Menorrhagia	71	(46.71%)	5	(20.00%)	8	(16.00%)	-	
2. Vaginal discharge	30	(19.73)	-		2	(4.00%)	12	(40.00%)
3. Pain in abdomen	10	(6.57%)	-		-		-	
4. Backache	10	(6.57%)	-		-		-	
5. Weight gain	-		-		8	(16.00%)	-	
6. Nausea & giddiness	-		-		8	(16.00%)	-	
7. Itching	-		-		-		5	(16.66%)
8. Pelvic Mass	8	(5.26%)	-		-		-	
9. Failure	4	(2.60%)	1	(5.00%)	3	(6.00%)	4	(13.33%)
10. Removal/ Discontinuation	11	(7.20%)	2	(10.00%)	5	(10.00%)	-	
11. Expulsion	5	(3.28%)	-		-		-	
12. Perforation	4	(2.63%)	1	(5.00%)	-		-	

Table V shows the comparision of various clinical side effects in women using different contraceptives which are described as follows:-

Menorrhagia : Maximum number (46.71%) of Copper 'T' users complained of Menorrhagia. 25% women having this complaint were loop users and 16% cases had menorrhagia while using

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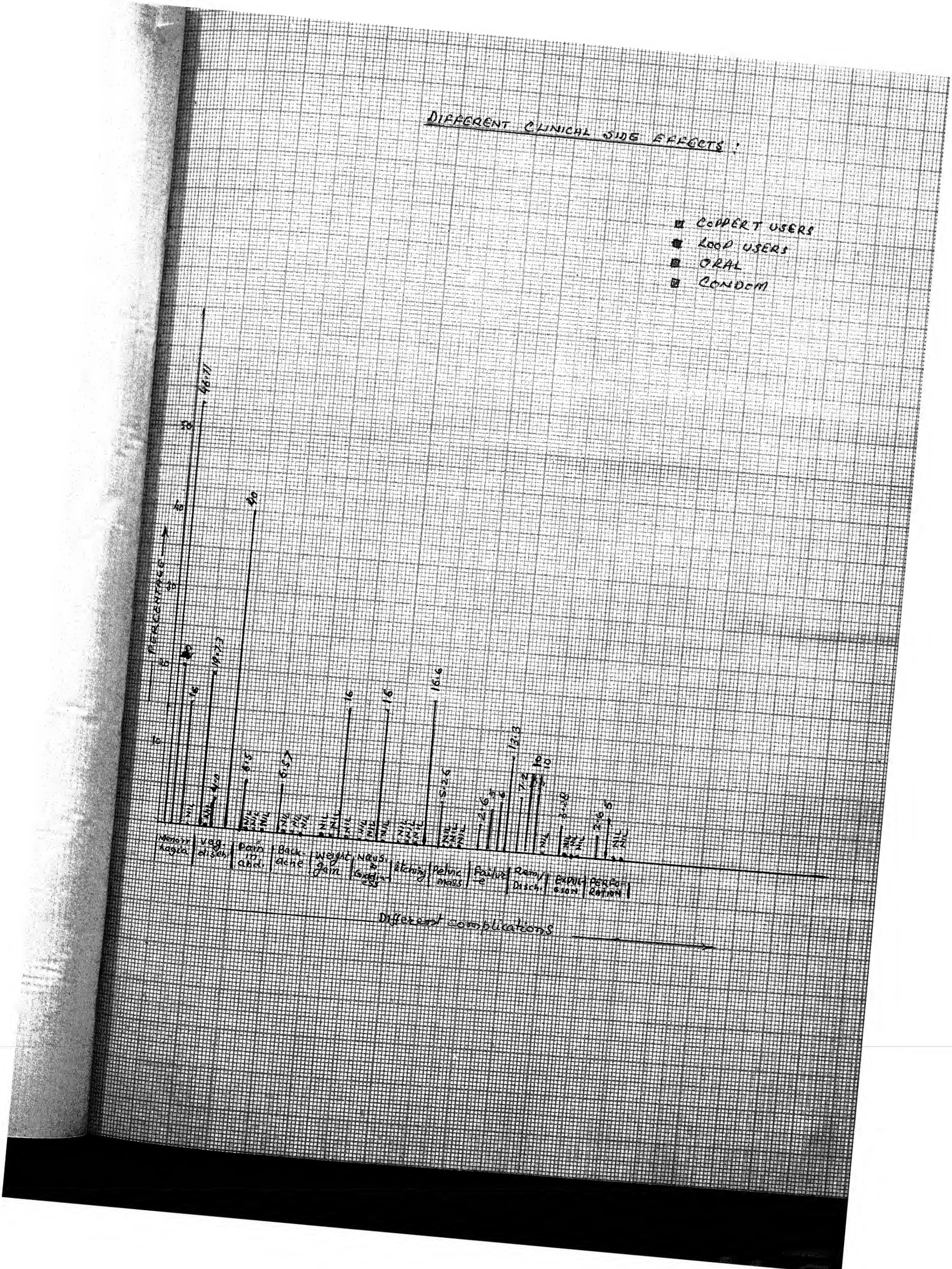
DIFFERENT CLINICAL SIDE EFFECTS :



P. T. O.

oral contraceptives. There was no such complaint in women having an opposite condom partner.

Vaginal Discharge : Maximum number (19.7%) of women who complained of Vaginal discharge were Copper 'T' users. Only 4% women had this complaints using on oral contraceptives. In 40%cases vaginal discharge was present in women with an opposite condom users partner.

Pain in Abdomen and backache : Only 6.57% women who were Copper 'T' users had pain in abdomen and backache. No such complaint was observed in women using other contraceptives besides Copper 'T'.

Weight Gain : 16% women complained of slight weight gain among the oral contraceptive.users. This was not complained by women on other contraceptive methods.

Nausea & giddiness : Similar number (16%) cases had this complaint while on oral contraceptive therapy.

Itching : 5 (16.66%) cases had itching in women with opposite condom user partner. IUCD and oral contraceptive users did not give any evidence of Itching.

Pelvic Mass : Only 5.25% cases had Pelvic Mass among the copper 'T' users. There was no evidence of only Pelvic mass in which women using Loop, orals are in women having a condom partner.

Failure rate : 13.3% women with an opposite condom users partner became pregnant and 2.6% of failure rate was observed among Copper 'T' users and 5% failure was in loop users. A high rate of failure 6% was observed among patients using oral contraceptives.

Removal/Discontinuation : 7.2% women among Copper 'T' users needed removal of the device due to bleeding and pains. 10% needed the removal among loop users and 10% women discontinued the using oral contraceptives due to pregnancy, forgetfulness and wanting another child.

Expulsion : 3.28% women expelled the Copper 'T' spontaneously.

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Perforation : 5% of perforations were seen in Loop users and 2.63% in Copper 'T' users. There was no such complaint in women using other contraceptives.

4. STUDY OF VAGINAL CYTOLOGY :

The vaginal cytological examination of all these women was also performed. The changes observed in the vaginal cytology of these women were:-

Dysplasia
Inflammation and
Infection due to Trichomonas vaginalis.

Dysplasia :

The association of dysplasia was shown with age and duration of use of the device in Table VI to Table XIII.

The Dysplasia observed was graded into 3 grades :

- Mild Dysplasia
- Moderate Dysplasia and
- Severe Dysplasia

(as discussed in Material and Method).

Dysplasia in Copper 'T' users : In 7.89% cases of copper 'T' users Mild dysplasia was observed at the age range of 30-34 years. About 9.20% of mild dysplastic changes were seen in the age range of below 20 years to 29 years. 3.94% of mild dysplasia was present at the age range of 35 years to above 40 years.

Only 2 cases of moderate dysplasia were observed among the Copper 'T' users. One was at the age range of 25-29 years and one at 30-34 years.

No case of severe dysplasia was present in the Copper 'T' users.

..... 58/-

Table VI : Showing rate of Dysplasia among Copper 'T' users according to Age

Age	Copper 'T' users	No. of Dysplasia observed			Rate per 100 of Dysplasia observed			Control group
		Mild	Moder-ate	Severe	Mild	Moder-ate	Severe	
Below 20 yrs	6	2	-	-	1.31	-	-	-
20-24 years	40	3	-	-	1.97	-	-	-
25-29 "	54	9	1	-	5.92	0.65	-	1(2.5%)
30-34 "	40	12	1	-	7.89	0.65	-	1(2.5%)
35-39 "	8	4	-	-	2.63	-	-	-
Above 40 yrs	4	2	-	-	1.31	-	-	-
	152	32	2	-	21.03	1.30	-	2(5%)

Table VII : Showing incidence of Mild and Moderate Dysplasia in Copper 'T' users according to duration of use.

Duration	Number of Copper 'T' users	No. of Dysplasia observed			Rate of Dysplasia		
		Mild	Moderate	Severe	Mild	Moderate	Severe
Initial	20	3	-	-	1.97	-	-
1-6 months	28	4	-	-	2.63	-	-
7-12 months	35	9	-	-	5.92	-	-
1-2 years	18	12	1	-	7.89	0.65	-
2-3 years	28	2	-	-	1.31	-	-
3-4 years	9	0	1	-	-	0.65	-
4-5 years	4	1	-	-	0.65	-	-
5-6 years	6	1	-	-	0.65	-	-
7-11 years	4	-	-	-	-	-	-
	152	32	2	-	21.02	1.30	-

..... 59/-

7.89% of mild dysplasia was observed after the use of Copper 'T' after 1-2 years. At 7-12 months 5.92% of mild dysplasia was present. 1.97% of mild dysplastic changes were seen in initial smears i.e. before the user of Copper 'T' Only 2 women showed moderate dysplasia after duration of 1-2 years and 3-4 years (Table VII).

Dysplasia in Loop Users : The maximum percentage (20%) of mild dysplasia was met in with women of higher age group i.e. above 40 years.

Table VIII : Showing rate of mild dysplasia among Loop users according to Age.

Age	No. of Loop users	No. of Dysplasia observed	Rate per 100	Control group
Below 20 years	0	-	-	-
20-24 years	8	-	-	-
25-29 years	4	-	-	1 (2.5%)
30-34 years	4	-	-	1 (2.5%)
35-39 years	0	-	-	-
Above 40 years	4	4	20%	-
	20	4	20%	2 (5%)

Table IX : Showing incidence of mild dysplasia among women using loop according to duration of use

Duration of use	No. of Loop users	No. of Dysplasia observed	Rate per 100
Initial	-	-	-
1-6 months	4	-	-
7-12 months	-	-	-
1-2 years	-	-	-
2-3 years	4	1	5
3-4 years	4	-	-
4-5 years	4	-	-
5-6 years	3	2	10
7-11 years	1	1	5
	20	4	20

***** 60/-

10% of mild dysplastic changes were observed after using the loop for 5-6 years. Equal percentage (5%) of dysplasia was seen at 2-3 years duration and 7-11 years of duration of use (Table IX). In no case moderate or severe dysplasia was seen.

Dysplasia in Oral Contraceptive Users:

No case of moderate and severe dysplasia was seen in users of oral contraceptives. 4% of mild dysplasia was seen in the women of 25 to 29 years, and 30-34 years. 2% of mild dysplastic changes were seen at the age group of 20-24 years and 35-39 years (Table X).

Table X : Showing rate of mild dysplasia in Oral contraceptive users according to age

Age	Total No. of women using oral contraceptives	No. of Dysplasia observed	Rate per 100	Control group
Below 20 years	-	-	-	-
20-24 years	14	1	2.0	-
25-29 years	18	2	4.0	1(2.5%)
30-34 years	14	2	4.0	1(2.5%)
35-39 years	4	1	2.0	-
Age above 40 years	-	-	-	-
	50	6	12.0	2(5%)

Table XI - Showing incidence of mild dysplasia in women using oral contraceptives according to duration of use

Duration	Total number of Oral users	No. of Dysplasia observed	Rate per 100
Initial	10	1	2.0
1-6 months	11	1	2.0
7-12 months	20	2	4.0
1-2 years	4	1	2.0
2-3 years	5	1	2.0
3-4 years	-	-	-
4-5 years	-	-	-
5-6 years	-	-	-
7-11 years	-	-	-
	50	6	12.0

Maximum percentage (4%) of women showing mild dysplastic changes among the users of oral contraceptives had taken the contraceptives for 7-12 months. duration. Equal percentage 2% of women had dysplastic changes at intial, 1-6 months after, and 1-2 years and 2-3 years of use (Table XI).

Dysplasia in women with an opposite condom user partners:

Mild Dysplasia was present in 1 case at the age of 35-39 years and after 10 years of duration of use.

Table XII : Rate of Dysplasia in women with an opposite condom user partner according to 'Age'

Age	Total no. of women with opposite condom user partner	No. of Dysplasia observed	Rate per 100	Control group
Below 20 years	-	-	-	-
20-24 years	6	-	-	-
25-29 years	12	-	-	1(2.5%)
30-34 years	7	-	-	1(2.5%)
35-39 years	4	1	3.33	-
Above 40 years	1	-	-	-
	30	1	3.33	2(5%)

Table XIII : Rate of Dysplasia in women with an opposite condom user partner according to duration of use.

Duration	Total No. of women with opposite condom partner	No. of Dysplasia	Rate per 100
Initial	-	-	-
1-6 months	3	-	-
7-12 months	3	-	-
1-2 years	11	-	-
2-3 years	3	-	-
3-4 years	2	-	-
4-5 years	-	-	-
5-6 years	4	-	-
7-11 years	4	1	3.33
	30	1	3.33

..... 62/-

Control Group :- There were only 2 cases of mild dysplasia present in the control group. 1 at the age range of 25-29 years and other at the age range of 30-40 years.

Comparision of Dysplasia seen due to use of different contraceptive devices at different visits with and without treatment.

A comparision of dysplastic changes was done in women using different contraceptives at different visits with treatment (Table XIV, Fig. 10) and without treatment (Table XV).

TABLE XIV

Showing comparision of dysplasia due to use of different contraceptives at different visits after treatment.

Name of the device	Total No. of women follow-ed	Dysplasia observed at 1st visit	Total No. of Cases of Dysplasia receiving treatment	After treatment: Dysplasia at 3 months after 1st visit	After treatment: Dysplasia at 3 months after 2 nd treatment	After treatment: Dysplasia at 3 months after 3rd treatment
Copper 'T'	152	Mild 32(21.05%)	27(17.7%)	25(16.44%)	16(10.52%)	
		Mod. 2(1.31%)	2(1.31%)	1(0.65%)	-	
		Severe -	-	-	-	
Loop	20	Mild 4(20.0%)	3(15.0%)	2(10.0%)	1(5.0%)	
		Mod. -	-	-	-	
		Severe -	-	-	-	
Oral Contracep-tives	50	Mild 6(12.0%)	4(8.0%)	5(10.0%)	3(6.0%)	
		Mod. -	-	-	-	
		Severe -	-	-	-	
Condom	30	Mild 1 (3.33%)	1(3.33%)	1(3.33%)	-	
		Mod. -	-	-	-	
		Severe -	-	-	-	
Control group	40	Mild 2(5.0%)	1(2.5%)	1(2.5%)	-	
		Mod. -	-	-	-	
		Severe -	-	-	-	

A total of 21.05% mild and 1.31% of moderate dysplasia changes were seen in Copper 'T' users at 1st visit. 27 cases

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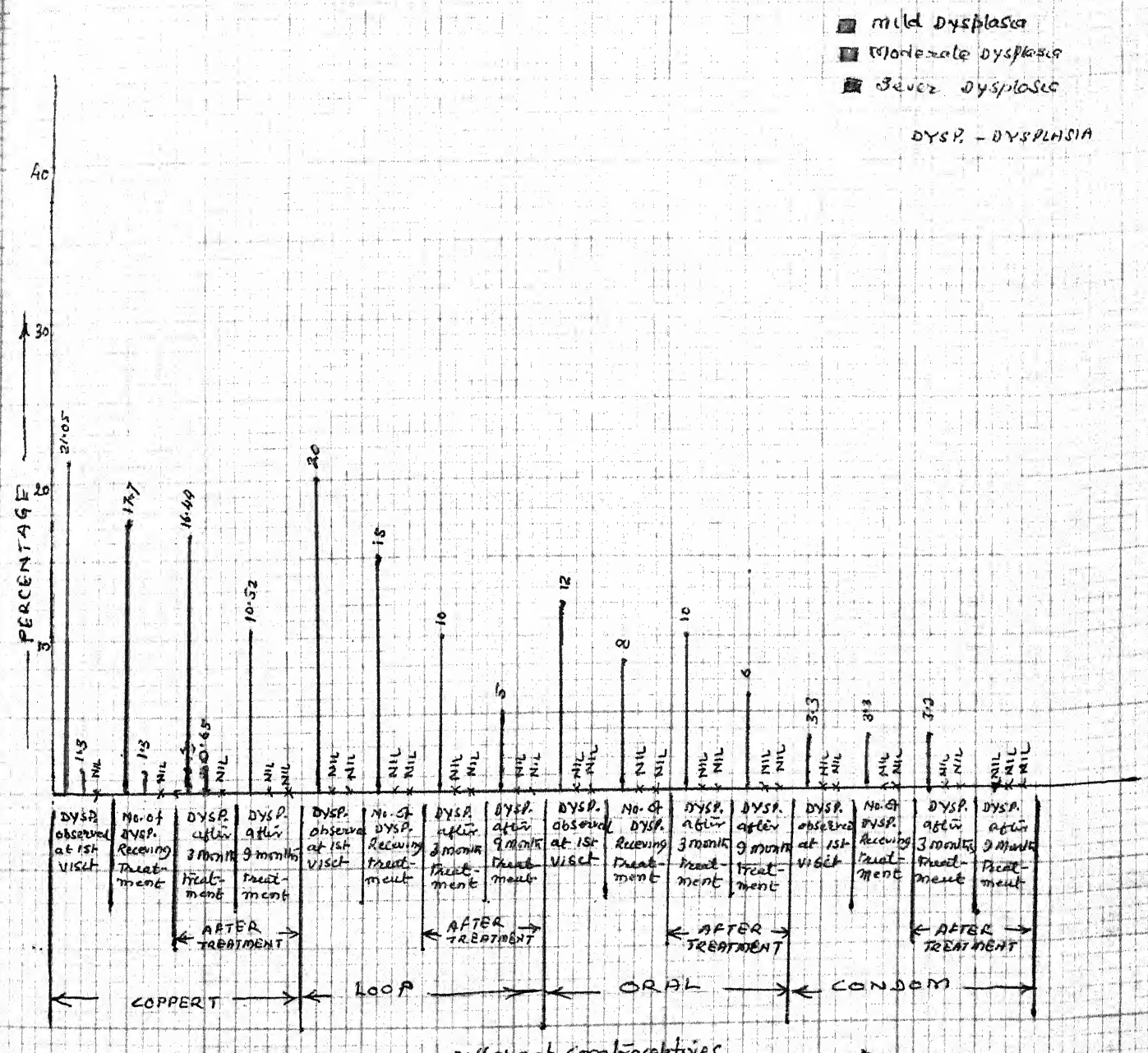
FIG 5

COMPARISION OF DYSPLASIA DUE TO USE OF DIFFERENT CONTRACEPTIVES AT DIFFERENT VISITS BEFORE AND AFTER TREATMENT :



showing mild dysplastic and 2 cases with moderate dysplasia were given treatment. In the next visit there was 16.44% of mild and 0.65% of moderate dysplasia seen in their vaginal smears. This further reduced to 10.52% after treatment at 9 months interval. There was no case of severe dysplasia observed throughout the study.

5 cases of Copper 'T' users, who were also showing mild dysplasia, were not given any treatment. A regression to inflammatory smear was seen in 1 case, another women had a negative smear and the remaining 3 had same mild dysplastic changes in the vaginal smear.

Table XV

Showing changes in dysplasia without treatment

Name of device	Total No. of women followed	Dysplasia observed at 1st visit	Total no. of cases of Dysplasia who were not given any treatment	Changes in Vaginal Cytology in follow-up smears: Negative Smear	Inflammation	Dysplasia
Copper 'T'	152	Mild 31(21.05%)	5(3.3%)	1 ←	1 ←	3 =
		Mod. 2(1.31%)	-	-	-	-
		Severe -	-	-	-	-
Loop	20	Mild 4(20%)	1(5.0%)	-	-	-
		Mod. -	-	-	-	1 →
		Severe -	-	-	-	-
Oral Contracep-tives.	50	Mild 6(12%)	2(4%)	-	-	-
		Mod. -	-	-	-	2 →
		Severe -	-	-	-	-
Condom	30	Mild 1(3.3%)	-	-	-	-
		Mod. -	-	-	-	-
		Severe -	-	-	-	-
Control group	40	Mild 2(5.0%)	1(2.5%)	-	-	-
		Mod. -	-	-	-	1(2.5%) →
		Severe -	-	-	-	-

Progression →
Regression ←
As such =

....64/-

20% of mild dysplastic changes were seen in women using loop. 3 women having dysplastic changes were given proper treatment. They showed a regression to 10% of dysplastic rate of 3 months and at 9 months,only 5% of mild dysplasia was left. 1 case who was not given any treatment showed progression to moderate dysplasia in the follow up vaginal cytology.

12% of mild dysplasia was observed among oral contraceptive users. 5% were given proper treatment. First there was a slight rise, 10% of incidence of dysplasia at the 3 months of duration but at the 9 months a regression (6.0%) in the incidence of mild dysplasia was observed. The remaining 4.0% patients were not given any treatment. They showed a progression to moderate from mild dysplasia in the follow up smears.

One woman with an opposite condom user showed mild dysplasia in her vaginal smear at the Ist visit. There was no change in her cytological pattern after treatment, after 3 months but at the IIIrd visit after 9 months there was no dysplasia left.

There was no evidence of severe dysplasia throughout the study period.

5% of mild dysplasia was also present in the control group. 2.5% of women having mild dysplastic changes were given treatment. A regression in the rate of dysplasia was present in the follow up smear to negative cytology.

One woman was not given any treatment. There was progression of mild dysplasia to moderate dysplasia which was evident in her vaginal cytology.

The inflammatory cells were also present in the vaginal cytological smears (Fig.24).

61.5% cases were showing inflammation among the Copper 'T' users. 74 women out of these 86 cases were given treatment and 12 women were not subjected to any therapy. The inflammation was seen to reduce after treatment. 43.4% of inflammation was present after 3 months and this further reduced to 25.0% at 9 months interval.

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Table XVI

Showing comparision of Inflammation due to different contraceptives at different visits after treatment.

Name of the device	Total No. of women observed	Total No. Inflammation at Ist visit	No. of women given treatment	After Treatment: Inflammation at IInd visit after treatment	After Treatment: Inflammation at IIIrd visit after treatment
		No. (%)	No. (%)	No. (%)	No (%)
Copper T	152	66(61.5%)	74(48.6%)	66(43.4%)	38(25.0%)
Loop	20	8(40.0%)	6(30.0%)	5(25.0%)	2(10.0%)
Oral Contraceptive	50	5(10.0%)	4(8.0%)	3(6.0%)	2(4.0%)
Women with opposite condom partner	30	12(40.0%)	9(30.0%)	7(23.3%)	5(16.6%)
Control group.	40	14(40.0%)	12 (30.0%)	8(20.0%)	4(10.0%)

Table XVII

Showing incidence of Inflammation in women using different contraceptives without giving any treatment

Name of the device	Total No. of women observed	Total No. of Inflammation at Ist visit	No. of women not given treatment	Changes in follow-up cytology without treatment: Negative Smear	Inflammation: Mild	Inflammation: Mod.	Inflammation: Severe	Dysplasia: Mild	Dysplasia: Mod.	Dysplasia: Severe
		No. (%)	No. (%)							
Copper 'T'	152	66(61.5%)	12(7.8%)	4(12.6%) ←		8(5.2%) =				
Loop	20	8(40.0%)	2(10.0%)	-		1(5.2%) =		1(5.2%) →	-	-
Oral Contraceptive	50	5(10.0%)	1(2.0%)	-		-		1(20%) →	-	-
Women with opposite condom partner	30	12(40.0%)	3(10.0%)	1(3.33%) ←		2(66%) =		-	-	-
Control group	40	16(40.0%)	4(10.0%)	-		2(50%) =		2(5.0%) →	-	-

Remained as such = Regression ← Progression →

In the 12 women, who did not take any treatment there was no change in the vaginal cytology of 8 women and 4 women showed a regression to negative smears.

40% of cases showed inflammation in the Loop users. 6 cases were treated and 2 were not given any treatment. A decrease of inflammation rate (10.0%) was seen in these patients also at 9 months time. Of the 2 women not taking any treatment, 1 women showed the same inflammatory changes in her vaginal smear and 1 progressed to mild dysplasia.

Equal percentage (40.0%) of cases showed inflammatory changes in women with an opposite condom partner. 9 cases were given prompt treatment and they showed a regression of inflammatory rate to 16.6% at 9 months duration. 3 women were not given any treatment. 1 case of these, showed a negative but the 2 women did not show any evidence of reduction of inflammatory rate.

Only 10.0% of cases showed inflammation in patients using oral contraceptives at the 1st visit. 4 women took treatment. 6% of inflammation was seen at 3 months duration after treatment. In the further follow-up after treatment the patients were showing only 4% of inflammation. 1 woman who did not take any treatment showed a progression to mild dysplasia.

40% of inflammation was observed in patients of the control group, at the 1st vision. Only 12 cases were given treatment. 20% of inflammation was present at 3 months interval and this further regressed to 10.0% on further follow up. 4 cases were not kept on any therapy. 2 cases did not show any change in their vaginal smears, whereas the other 2 progressed to mild dysplasia.

Table : XVIII (Fig 8 and 13).
showing comparison of Trichomonal Infection due to different contraceptives, at different visits before and after treatment

Name of Device	Total No. of women observed	Trichomonal Infection at 1st visit	Infection at 3rd visit at 3 months	Infection at 9 months
Copper 'T'	152	24 (15.7%)	16(10.52%)	8(5.2%)
Loop	20	-	-	-
Nil	20	2 (4.0%)	-	-
Oral steroids	50	12(40.0%)	11(36.66%)	8(26.66%)
Condom	30	6(15.0%)	4(10.0%)	2(5.0%)
Control group	40			

The vaginal smears showed presence of Trichomonas vaginalis in some patients. Maximum percentage (40%) of

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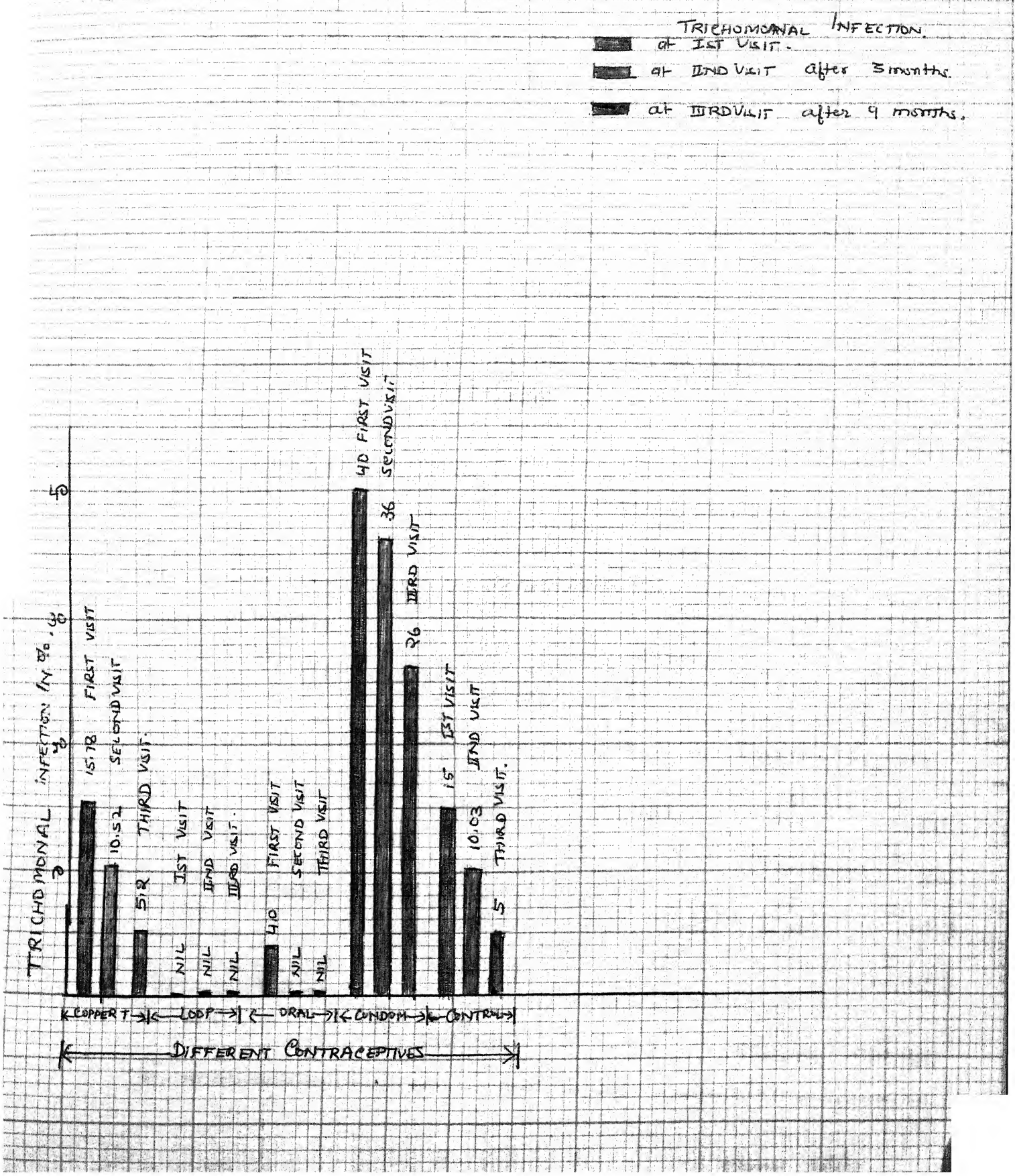
FIG 6.

TRICHOMONAL INFECTION DUE TO DIFFERENT CONTRACEPTIVES AT DIFFERENT VISITS.



Trichomonas vaginalis was seen in the women with an opposite condom user partner. These patients were treated with and after 3 months there was 36.66% Trichomonal vaginalis and in the 3rd visit there was 26.66% incidence of infection.

15.78% infection with Trichomonas vaginalis was observed in the women using Copper 'T'. After 3 months 10.52% of infection remained. This further reduced to 5.26% after 9 months.

Only 4% of Trichomonas vaginalis were observed in women on oral contraceptives. There was no evidence of infection in the follow up smears.

15% of Trichomonal infection was present in the control group and these patients in the follow up smears showed a regression. At the IIIrd visit at 9 months interval only 5% of incidence of infection remained.

Table XVII : (Fig. 14)

: Distribution of women according to Histopathological pattern by the user of different contraceptives.

Name of Device	Total no. of patt-women in wh-om BS was done	Normal	Cystic-Hyperpl-asia	Chronic-Endomet-ritis	Stromal-oedema	Inadequate Endometrium
		No. %	No. %	No. %	No. %	No. %
Copper 'T'	100	84 (84.0%)	-	2 (2.0%)	6 (6.0%)	8 (8.0%)
Loop users	6	4 (66.66%)	-	-	1 (16.66%)	1 (16.66%)
Oral contracep-tives	36	22 (61.11%)	4 (11.11%)	4 (11.11%)	2 (5.55%)	4 (11.11%)
Women with an opposite condom user partners.	14	12 (85.71%)	-	-	-	2 (14.28%)
Control	12	8 (66.66%)	-	-	2 (16.66)	2 (16.66)

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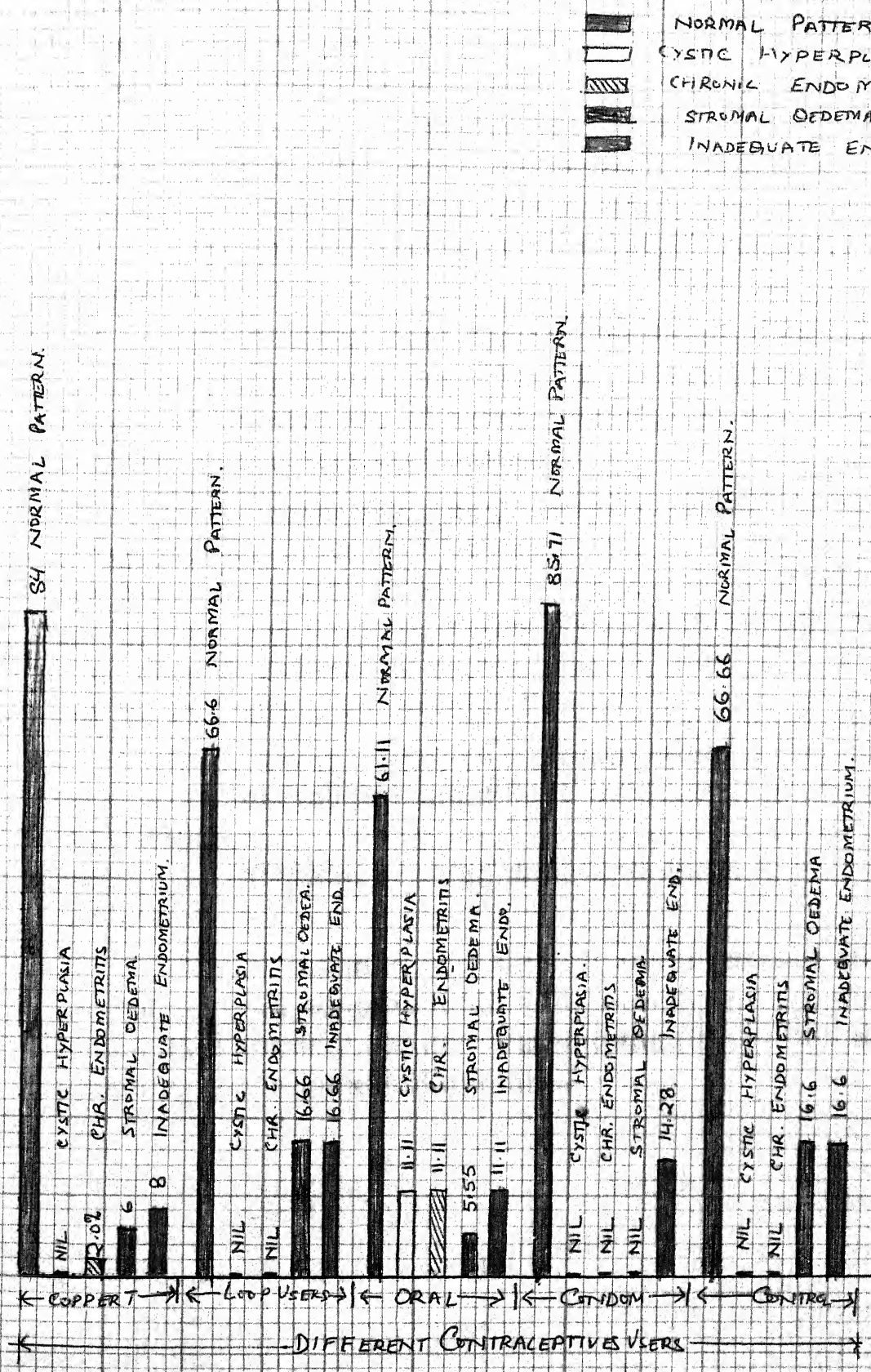
FIG 7

DISTRIBUTION OF WOMEN ACCORDING TO HISTOPATHOLOGICAL PATTERN AFTER USE OF DIFFERENT CONTRACEPTIVES.



At the XXIxd visit i.e. at 9 months periods Endometrial biopsy was also done in the women using different contraceptives and the different patterns of the Endometrium obtained are shown in Table XVII.(Fig 14).

Endometrial biopsy was done in 100 women, out of the total 152 Copper 'T' users. 84% showed a normal Endometrium i.e. Secretory or Proliferative phase. 8% had an inadequate Endometrium. 6% had stromal oedema and 2% had chronic Endometritis.

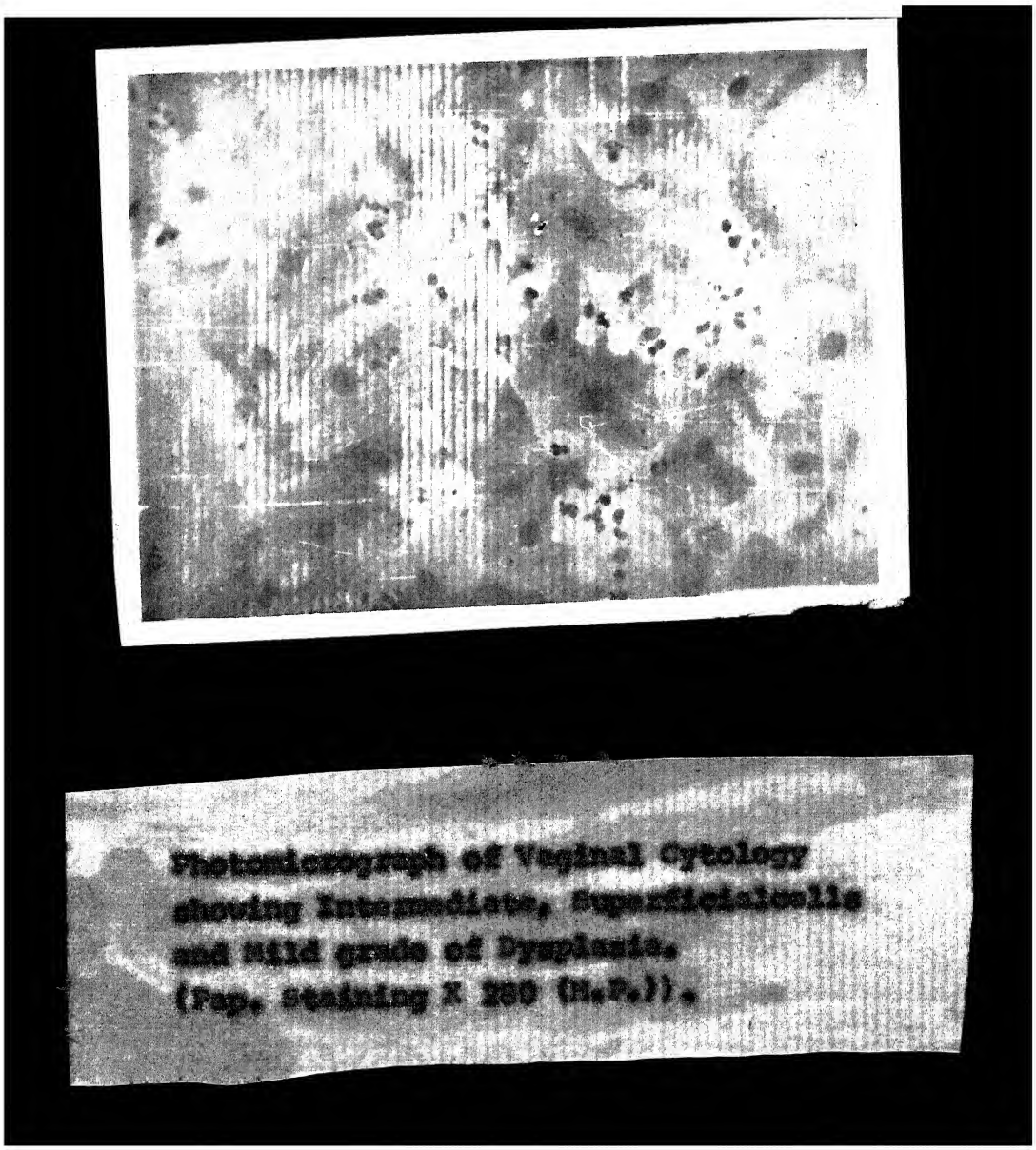
Only 6 women, came for the Endometrial biopsy among the Loop users. There was a normal pattern obtained in 4 cases and 1 woman showed stromal oedema. In the other case, the endometrium was inadequate.

In 36 women using oral contraceptives, Endometrial biopsy was done. In oral contraceptive users normal pattern was found in 61.11% cases; while 11.11% cases showed Cystic hyperplasia and Chronic Endometritis. 5.55% women showed only stromal oedema. No opinion can be made in 11.11% cases due to inadequate Endometrial biopsy.

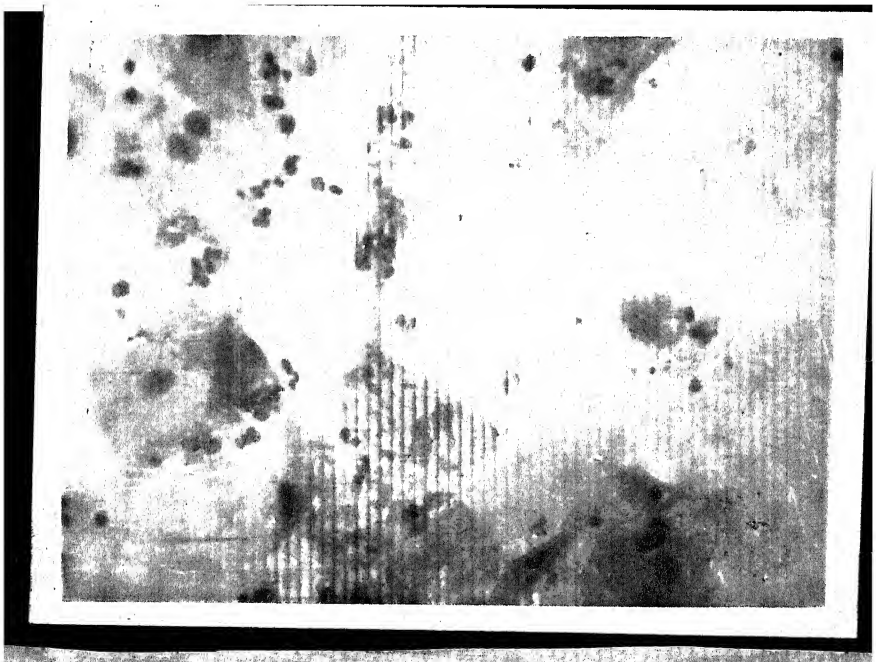
In patients having an opposite condom user partner, Endometrial biopsy did not reveal anything significant. 85.7% cases were showing normal proliferative or secretory pattern of endometrium while in 14.28% cases biopsy was inadequate.

Only 12 women of the control group offered themselves for endometrial biopsy. 66.6% patients showed a normal Endometrial pattern. 16.6% was stromal oedema and in the remaining inadequate endometrium.

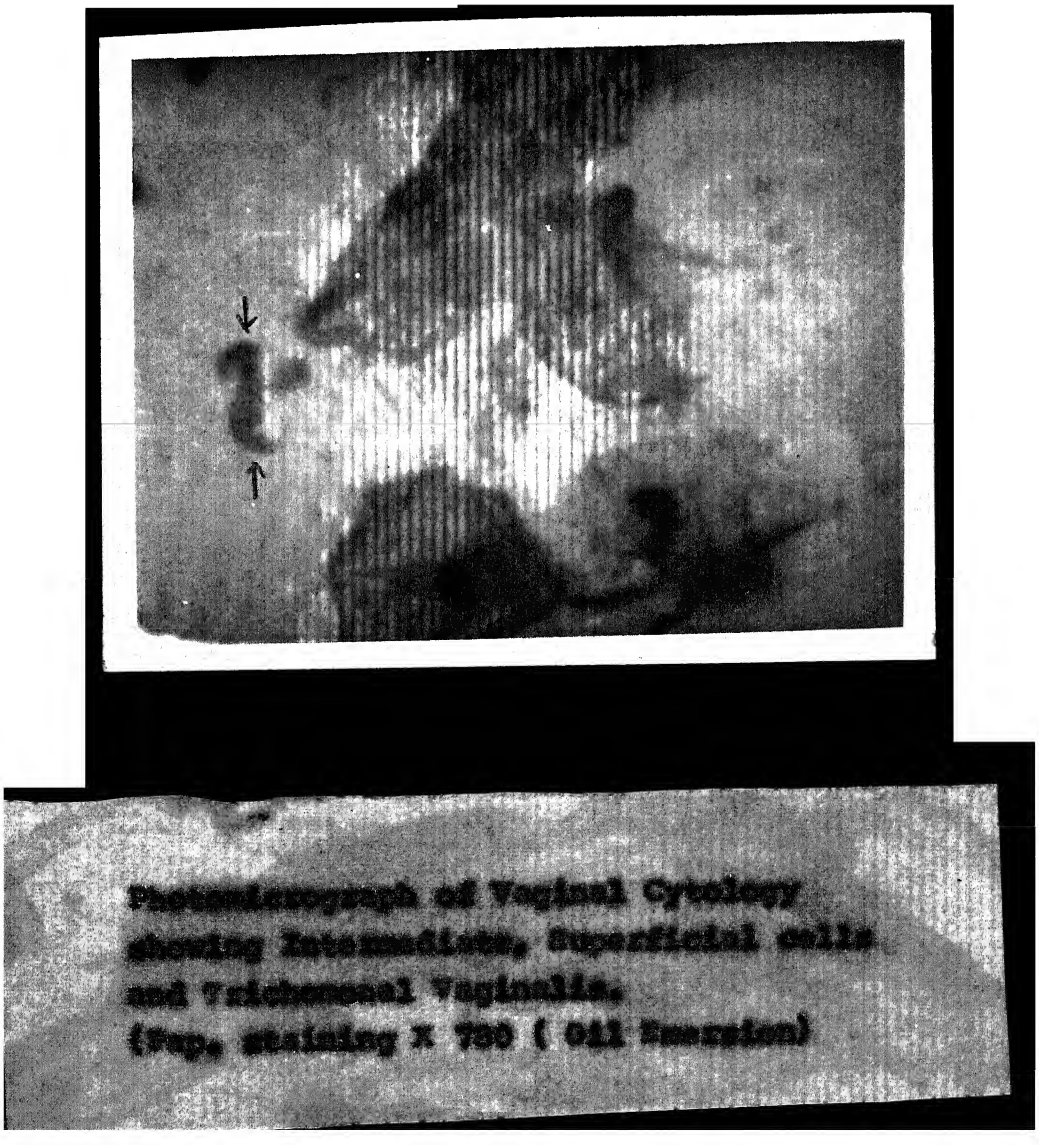
PHOTOGRAPHS



Photomicrograph of Vaginal Cytology showing Intermediate, Superficialcells and Mild grade of Dysplasia. (Pap. Staining X 200 (H.P.)).



Photomicrograph of Vaginal Cytology showing Intermediate, Superficial cells and Moderate Grade of Dysplasia.
(Pap. Staining X 200 (H.P.)



Photomicrograph of Vaginal Cytology showing Intermediate, Superficial cells and Trichomonal Vaginalis.
(Pap. staining X 720 (Oil Immersion)

DISCUSSION

DISCUSSION

There is no doubt that no single method can be utilised for birth control of the population in our country because different areas have different socio-economic conditions, educational standards, customs and thinking and different means of treatment.

Experiences over the last two decades has shown a great deal of variation in the results of clinical trials and cytological findings of oral contraceptives and other contraceptives (Hines and Goldzieher, 1969). The reasons for such variations are complex. In part they may result from differences in the ethnic group or socio-economic characteristics of the population studied from differences in the study designs or from differences in the approach to data analysis.

Variations in the performance of the same IUCDs in different countries and different clinics can be expected, since various factors are responsible e.g. meaning not clear

(i) Patient Population :

Differences of means, ages, parity, gravidity and last gestation.

(ii) Physicians experience:

Physicians with less experience and skill in IUCD insertion are more likely to have a lower incidence of correct high fundal positioning with resultant higher risk of expulsion and pregnancy.

(iii) Side effects and Tolerance :

Vary among different women.

(iv) Clinical attitudes

The rate of removals for bleeding and pain, may be influenced by the attitudes of the physicians and other members of the staff.

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(v) Additional contraceptives:

Availability of other methods.

In the present study the results of the 3 types of temporary contraceptives, namely:

IUCD - Copper 'T'
- Lippes Loop
- Oral contraceptives and
- Condom

have been compared.

AGE :

Most of the women using the above mentioned contraceptives were between the age range of 20 years to 34 years. The youngest was of 20 years and the oldest was above 40 years of age.

Majority of the women using the different contraceptives were in reproductive age group mainly (20-35). Mostly the women were Copper 'T' users. Majority of the women using different contraceptives were within the age group of 21-35 years, although a good percentage of women upto the age of 40 years seemed to be using the Lippes Loop. Women of higher age group were mostly using Condom.

These findings were found to be in accordance with the study of Affandi and Vichai, 1976. They studied 200 women using Copper IUCD. The youngest women in their study group was of 18 years and the oldest women was 47 years of age. Similar findings were reported by N.N.Roy Chowdhury, etal, 1966.

PARITY :

Distribution of women using different contraceptives in relation to parity is shown in Table XV.

Mothers of 1-4 children were seen to use these contraceptives to the maximum.

..... 69/-

Among Copper 'T' users there were 2 nulliparous women using the device while no other mean of contraception was opted for by the nulliparous women in the present study. It was also observed that women having more than 4 children used the device as a means of family limitation rather than for spacing.

All the nulliparous women, studied in this work were using the Copper 'T' as a contraceptive device. Women with one or 2 children were mostly using the oral contraceptives and with a parity of 1 to 3 children the women were using copper 'T' and Lippes Loop. But as the parity advanced beyond 3 i.e. women having 3 or more children preferred to use condom as a contraceptive means.

In the study of Affandi and Vithar 1976, in the 200 women using Copper IUCD, there was no nulliparous women in the series. 24 women had one child and the rest were multiparous.

Roy Chowdhury and coworkers 1980 reported that with respect to the Parity it appears that mothers of 1 to 4 children were maximum users of modern contraceptive means.

So, the distribution of women, according to Age and Parity were comparable in all the four groups of women using different contraceptive methods.

CLINICAL SIDE-EFFECTS

Menorrhagia :

Maximum number (46.7%) of Copper 'T' users complained of Menorrhagia i.e. these patients complained of excessive amount of bleeding with a prolonged duration of blood-flow. 25% of loop users complained of Menorrhagia and only 16% women had this complaint while they were using oral contraceptives. No women with an opposite condom user partner complained of Menorrhagia though they suffered from pelvic infection and cervical erosion.

..... 70/-

So, Menorrhagia was seen maximum (46.71%) in the Copper 'T' users. This finding was similar to the studies done by Malmquist, etal (1974) and Guillebaud, etal (1978). They reported a prolonged duration of flow in women using IUCDs.

Zador, etal (1976) and Wan and Colleagues, (1977), also reported, that in comparison to Lippes Loop, the duration of flow is slightly more in Cu-IUCD users. The duration was prolonged from 0.5 to 1.5 days for Cu-IUCD users.

According to Daniel Mishell (1979) about 50-60 ml. of blood is lost per cycle in Cu-IUCD users.

16% of oral contraceptive users complained of Menorrhagia. This was very unlike the study of Hafnawi, etal (1975) and Hafnawi and co-workers, (1977). They suggested a reduction in the mean blood levels of oral steroids.

Zanartu and Navarro (1968) noted that in 130 women on oral steroids, uterine bleeding remained normal in 27, was decreased in amount or duration in 47, was increased in 22 and was very irregular in 24.

Weight Gain:

Only 16% of oral contraceptive users complained of weight gain.

Hannecker, etal (1968), Rubio and Gonzalez (1970) also showed weight gain in their studies by use of oral contraceptives. Mishell and associates (1968) and Zartman (1970) have reported the same. Same was observed by Spellacy and colleagues (1970, 1972) and Gladwyn Leiman (1972).

No change in weight was observed among women using any other contraceptives i.e. in Copper 'T' users and women with an opposite condom partner.

Pelvic Mass :

5.26% women, who were Copper 'T' users showed the presence of Pelvic mass on per vaginum examination. No case

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was observed in oral contraceptives users.

Studies by Lippes (1963) and Tietze (1966) showed pelvic infection rates in IUCD users ranging from 0.6 to 3.5% per year.

The findings of the present study were in accordance with the work of Wright and Laemmle (1968), who found a five fold increase in the acute salpingitis rate in IUCD users versus oral contraceptive users. Eschenbach, etal, in 1977, reported that the risk of acute salpingitis was 4.4 times higher in IUCD users than the non-users. So, according to Eschenbach, etal (1977), both barrier methods (like condom) and oral contraceptives reduce the risk of developing acute salpingitis. This was observed in the study, as there was no case of salpingitis present in women with an opposite condom user partner and in users of oral contraceptives.

This tail of IUCD had been suggested as another explanation of the increased incidence of infection in IUCD users, so it was found more in IUCD users.

Pharriss (1970) observed inflamatory rate higher in the first two months immediately after the insertion of IUCD than later. In our series also the maximum cases were seen in the first six months of use.

Failure Rate:

(Due to pregnancy)

Maximum percentage (13.33%) of failure rate was observed in women with an opposite condom user partner and 6% of failure rate was seen in oral contraceptive users. 5% of failure rate existed in women using Loop. Least failure (2.6%) percentage was observed among Copper 'T' users.

Improper insertion and displacement of an IUCD has been shown to result more often in perforation, expulsion, removals (for pain and bleedings) and pregnancy by Tatum, (1975), Hasson, etal (1976) and Perlmutter, (1978).

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In contrast to reports by several workers (Shive and Thompson 1974, Perimutter, 1978) immediate post aboral insertion of a device or insertion upto 8 weeks post-partum is associated with increased pregnancy rate, the present study did not show a high pregnancy rate after IUCD insertions.

The possible reason for failure can be technical problems, regarding uniformity of the release rate of Copper and restricted life span of the device.

Failure on account of Removal of the device or discontinuation of oralet

11% of the removals were observed among the Copper 'T' users and 2% among the Loop users, 5% of women discontinued using the pills.

The removal of the device was attributed mainly to the bleeding and pain.

Trobough (1978) had given an average of 10% of pelvic pain with the small Cu-IUCDs.

Tatum, etal (1973, 1975) and Van Os (1978) gave results that increased pain, bleeding and removal rates were directly proportional to the size, shape, consistency and volume of the IUCD.

Only 5% of discontinuation rates were observed among the users of oral contraceptives. Inspite of having the highest theoritical effectiveness of the reversible methods of contraception, oral contraceptives have some failure rates as seen in some barrier methods.

Discontinuation rates as high as 50-60% were seen in some family planning clinics as reported by Hatcher, etal (1980).

Discontinuation of the therapy was due to menstrual irregularities or forgetting to take the pill at the same time everyday.

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Expulsions

3.20% of women using the Copper 'T' expelled the device spontaneously.

Kamal, etal.(1973), explained that disoriented or misplaced device and a dimensional disproportion can emite uterine irritation which provoked myometrial contractions causing the expulsion.

Even in well selected cases the shape of the uterine cavity was constantly under going change.

Mann, (1962) reported that during menseuration fundal hypertonia co-exists with isthmic hypotonia to constconditions in which the transverse diameter of the fundus was reduced while that of the isthmic tonicity was reversed in the post ovulatory phase of the menstrual cycle. Hence, it was difficult to achieve exact fitting and this lead to expulsion, (Hasson etal, 1976). In postental cases, expulsion was more due to a patulous-os and changes in dimensions of uterine cavity.

Perforations

5% (the rate is high, because of the less number of cases in the present series) of Perforation of uterus was seen among patients using the Lippes loop and only 2.63% of perforation were seen with the Copper 'T' users.

According to Mishell (1979), the perforation rates for the Copper 'T' and loop in a large multiclinical studies are almost in the same range of those for the Loop 1:1000 insertions.

Tatum (1976), identified 4 variables that influences the risk of fundal perforations.

(i) Size, shape and consistency of the device.
(ii) Status and configration of the device.
(iii) Insertion techniques, and
(iv) The skill and experience of the operator.

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Lippes (1979) observed 'Intrauterine contraceptive device do not perforate, for this to happen we need a practioner." Most of the fundal perforations occur or being at the time of insertion.

Cervical perforations result from downward displacement of the device, this could occur with any device with a vertical arm such as the 'T' or '7' devices. Nishell (1979) reported it to range between 1:600 to 1:1000 insertions.

No such complaint existed in women on oral contraceptives and women having an opposite condom partner.

Giddiness:

16% of women experienced giddiness while using the oral contraceptives. This symptom was never present in the copper 'T' of loop users or women with an opposite condom user partner.

Chinnatamby (1971), also noticed giddiness in her patients using oral contraceptives.

Summarizing and comparing the events at the end of the study period of one year, Copper 'T' showed best results followed by oral contraceptives and Lippes Loop (Table XV).

However, the difference is not statistically significant due to relatively small number of patients in each group.

Study of Vaginal Cytological Changes

Vaginal cytological smears of the women using different contraceptives revealed the following changes namely:-

Dysplasia of mild and moderate grade, inflammation and trichomonal infection.

Dysplasia:- There were only 2 cases (5.0%) of mild dysplasia in the control-group. No case of moderate or severe dysplasia was observed in the control group.

Dysplasia in IUCD Users:

In Copper 'T' Users:

A total of 21.05% of mild dysplastic changes were seen in the Copper 'T' users.

In 7.89% cases of Copper 'T' users mild dysplasia was observed at the age range of 30-34 years. 9.20% of mild dysplastic changes were seen at the age range below, 20 years to 29 years. 3.94% of mild dysplasia was seen at the age range of 35-40 years and above.

Only 2 cases of moderate dysplasia were seen in the Copper 'T' users. Only one was at the age range of 25-29 years and one at 30-34 years. There was no case of severe Dysplasia throughout the study.

7.89% of mild dysplasia was seen after 1-2 years of the use of Copper 'T'. 1.97% of dysplastic changes were present in the preinsertional smears. 3.55% of mild dysplasia was seen after 1 month to 1 year of use. 1.31% of mild dysplasia was observed after 2-3 years and 1.30% of mild dysplasia was seen after 4-6 years of use. Only 2 women showed moderate dysplasia after 1-2 years and 3.4 years of use.

In Loop Users:

Approximately equal to Copper 'T' Users i.e. 20% of mild dysplastic changes were seen in the loop users. Dysplastic changes were not observed in the initial smears. There was no case of moderate or severe dysplasia although the study period.

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The mild dysplasia was seen in women above 40 years. 5% of mild dysplasia was observed after 2-3 years and 10-11 years. 10% of mild dysplasia was present after 5 years above.

Ishihama and Nagaba (1964) in combined histo-cytological study, Ayre (1965) in cytological study had reported only a few instances of dysplasia in women using different intra uterine devices for varying periods.

After 3 months the women using Copper 'T' reported for follow up after treatment. A regression was observed in the dysplastic rate. Only 16.44% of mild dysplasia was seen in Cu 'T' users and only 1 case of moderate dysplasia was present. At the 3rd visit, i.e. at 9 months duration after further treatment, a further regression was observed. No case showed moderate or severe dysplastic changes and only 10.5% of women were left with mild degree of dysplasia. Out of the cases who were not given any treatment among the Copper 'T' users, showed a regression to negative smear and 1 showed only inflammatory changes while the remaining 3 cases did not show any change from mild dysplasia. This proved that the copper provided a protective covering against development of dysplastic changes.

The loop users also showed a regression of dysplastic changes after treatment. At the 3rd visits, at 9 months of duration, only 1 patient showed mild dysplastic changes and there was no case left with moderate or severe dysplasia. 1 case of loop users was not given any treatment. She showed a progression to moderate dysplasia in her follow up smear.

In the present work, it was observed, that those cases, who had inflamation in the initial smear (i.e. proinsertional smears) showed dysplastic smears at the 6 monthly examination. The inflamation was treated and the subsequent smears were normal i.e. Dysplastic changes were seen more from 6 months to 1-1/2 years of duration.

Most of the dysplastic smears were having accompanying infection. So patients having inflammation were promptly

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treated with local and oral antibiotic therapy intra vaginal tablets of NFP were also prescribed. There was a resultant regression of dysplasia after treatment, but without treatment there was progression of dysplasia in Loop users.

Cytological studies of Schwartz etal (1967), Sagiroglu and colleagues (1970) had reported incidence of dysplasia almost equal to control group. Most of the dysplasia showed a regression to normal at their follow-up, 6-12 months later. This was evident in the present study also.

Tietze (1966) had observed cytological smears of women at insertion ofIUCD and after 6 months of use and has reported transition from negative to dysplasia in 1% of cases and appearance of carcinoma in situ in 4% of the 4800 women examined. He also reported regression of these dysplastic changes.

Wahi etal (1968) reported that lesser time is required for progression from mild to moderate dysplasia in IUCD cases as compared to control group. This was also observed in the present work.

The findings of the present work were in accordance to the findings of Affandi and Viskar (1976)m, who followed 200 women by cytological smear examination using copper device for contraception. The study was conducted for a period of 4 years. They reported 5 smears of mild and 3 smears of moderate dysplasia. These cases with dysplasia showed a regression to normal in the follow-up smears in a period of one to 2 years after treatment.

Other workers also reported similar findings.

Misra etal (1977) carried out comparative cytological studies in 110 women using Lippes Loop and 90 women with Cu-IUCD for a period ranging from 3 to 5 years. No case of severe dysplasia or malignancy was found in either group on follow up. The incidence of dysplasia was slightly lower in Copper 'T' users than in loop users. This suggested that the Copper coating on the device somehow affords protection from occurrence of dysplasia. This supposition gained strength from

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the fact that all 6 initial dysplasias, 3 pre-insertional and 3 noted at first smear, regressed to normal within 6 to 12 months of copper contraception. Similarly 6 of the 11 dysplasia detected in follow up smears during 6 months to 3 years use of the device, regressed to normal on follow up 6 to 12 months later.

Luthra, etal (1980) had reported, their experience with the use of copper devices for 48 months. 30 women had dysplasias in the smears initially before insertion and equal number developed dysplasia during the follow up. The regression rate was almost 60% to 75% with all cases of dysplasias, by the end of 60 months.

Similar results were obtained in the following study of Aihat and colleagues (1980). They reported the results of long term effect of Copper intrauterine contraceptives devices on cervical epithelium, and endometrium 833 women using copper IUCDs were studies. There was mild dysplasia in 3 and moderate in 2 prior to insertion. However, some regressed within 6 months of follow up. Dysplasia (all mild) which occured during follow up regressed within 6-12 months.

In the study of Roy Choudhary and coworkers (1980), 4 cases of mild and 1 case of moderate dysplasia was present in 120 Loop users and 3 cases of mild and 2 cases of moderate dysplasia was observed out of 120 copper 'T' users. Duration of use in these cases was 24 months, there was no case of severe dysplasia even in users of longer duration. 2 women developed during the study period. Dysplasia regressed by the treatment, in all cases.

Dysplasia in Oral contraceptive users:

12.0% of cases using oral contraceptives showed mild dysplastic changes in the study group. There was no case of moderate or severe dysplasia seen through out the study.

4% of mild dysplastic changes were observed in the cytological specimen of women using oral contraceptives at the age range of 25-29 years and 30-34 years. 2% of

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dysplasia was present at the age range of 20-24 years and 35-39 years.

4.0% of mild dysplasia was seen after 7-12 month of use. 2% of mild dysplasia was present in pre-insertional smears and 2% of mild dysplasia was observed after 1-6 months 2-3 years and 3-4 years.

A gradual regression of dysplasia was observed in the follow up of vaginal cytology, in 6 women after treatment. In the 2nd visit i.e. after 3 months duration an increase in dysplastic changes to 12.0% were noted. A further treatment was given and a regression in dysplasia was observed to 6.0% at the 3rd visit, at 9 months duration. 2 women were not given any treatment. The vaginal cytology of 1 woman remained same but that of the other showed progression to moderate dysplasia. The present study had finding similar to the findings of following workers

Attwood (1966) stated that among 500 medicated women there was a 22% incidence of dysplasia whereas among 9000 controls there were only a 0.8% of incidence of dysplasia.

Liu etal (1967) noted 10% incidence of abnormal smears from 1000 women treated with hormones for contraception.

Melamed and coworkers (1969) also revealed an increase in the prevalence of severe dysplasia in steroid users.

Kline,etal (1970) in their study on 2296 women on contraceptive therapy, found a typical cells in smears in contrast to 17,734 women (control) in whom the incidence was 1%.

In this study by Wallach and colleagues (1970), on 385 patients on oral contraceptives they noticed cervical dysplasia in 11 patients and dysplasia with focal carcinoma in situ in one patient.

These changes and results were similar to those found in the general population of Agra. Vahidetal (1972) in their study at Agra studied a total of 26,110 smears out

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of which 1,641 showed various degree of dysplasia. The incidence of dysplasia being 6.29% Ketwani (unpublished study) reports a decreased incidence of 2.1% in 11,642 smears.

S.Mali and coworkers observed in Agra in 275 oral contraceptives dysplastic lesions of varying degrees were present in 17% women and only 6.9% of controls had dysplastic lesions. These women were on oral pills for a long time. No case revealed severe dysplasia or malignancy. There was a regression in the incidence of dysplasia by treatment.

Dysplasia in women with an opposite condom partner.

Dysplastic lesions were seen only in 2 cases out of 30 at the age range of 35-39 years. Subsequently no dysplasia was observed after treatment. There was no case of moderate or severe dysplasia.

Exactly similar findings were seen in the vaginal cytology of patients by N.N.Roy Choudhary (1980). No case revealed moderate or severe dysplasia. 2 cases showed mild dysplastic lesions. This dysplasia also regressed to normal.

So in all the contraceptive methods adopted, increased tendency to dysplasia was found in study group than controls. Approximately equal number (21.05%) and (20%) of mild dysplasia was observed in Cu and loop users. 12% of dysplastic changes in oral contraceptive users and 3.33% of mild dysplasia was observed in women with an opposite condom user partner.

These dysplastic changes were regressable after prompt and proper treatment. These changes were also regressable after discontinuation or removal of the device. In copper 'T' users these dysplastic changes regressed even if the device was left in situ and no treatment was given, as copper provided a protective coating.

INFLAMMATION AND TRICHOMONAL INFECTION :

Patients showed marked inflammatory changes in the vaginal cytological smears. This inflammation accompanied the dysplasia in most of the cases. Infection with Trichomonas

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vaginalis was also present in the vaginal smears. Proper intra-vaginal ITP Tablet was given to the patients. Local antibiotics and oral antibiotics were also prescribed. Due to the presence of inflammation, prompt treatment was advocated to the patients. There was a reduction in the incidence of inflammation and infection due to treatment. The dysplasia was present due to this associated infection. As a result of reduction in the infection, dysplasia also regressed by treatment.

In the present work, 61.5% cases of inflammation was seen in Copper 'T' users, 40% of women showed inflammatory changes in Loop users, women with the condom user partner and also in the control group. In the women using oral contraceptives, only 10.9% of cases showed inflammation. There was a gradual reduction in the incidence of inflammation (old and developed) in all groups including the control group after treatment. At the XXIInd visit, at 9 months duration 25.0% of cases of Copper 'T' showed inflammation 16.6% of cases showed inflammatory changes in the women with opposite condom user partner, only 4.0% cases were left having inflammatory changes among users of oral contraceptives. 10.0% of inflammatory cases were seen in Loop users and the control cases. These changes were seen in patients of all groups who were given treatment.

12 women having inflammation among the Copper 'T' users were not given any treatment. 4 cases showed a negative cytology whereas 8 showed the same inflammatory smear in the follow-up smears. 2 cases with inflammatory changes among Loop users were not given any treatment. 1 case showed the same cytological findings upon follow-up while the other showed evidence of dysplasia. 1 case among the oral contraceptive having inflammation did not take any treatment. She showed progression to dysplasia. 3 women with an opposite condom user partner were not subjected to any therapy. 2 women showed same inflamatory changes while 1 women showed

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evidence of dysplasia in her cytology. 4 cases of the control group who were not given any treatment, 2 showed old inflammation and 2 showed dysplastic changes in the cytology. Thus there was a progression to dysplasia without proper treatment.

Trichomonal infection was also seen in women using different types of contraceptives. Maximum percentage (40%) of Trichomonal infection was present in women with opposite condom user partner. This regressed to 26.66% after treatment in the follow-up smears.

15.78% of cases of the Copper '7' users showed Trichomonal in their vaginal smears which reduced to 5.26% cases in the 2nd visit at 9 months duration. No such incidence was present in loop users. Only 4% cases showed evidence of Trichomonas in the vaginal smears among women using oral contraceptives, by treatment the smears obtained after treatment were free of the Trichomonas.

15% of Trichomonal vaginalis were present in the control group they also showed a regression after treatment to 5%.

Many workers also reported a reduction in the incidence of inflammation. So the findings of the present study were found to be in coincidence with the work of various workers.

Affandi and Vizhar (1976) have reported that there was a reduction in the incidence of inflammation in their study on 200 women using IUCD. They also explained that the problem of infection can be avoided to a great extent by genital screening of the new patients and eliminating or treating those with existing infection before insertion of the device. There were 3 smears of moderate dysplasia with accompanying inflammation. This was curable after treatment.

Misra etal (1977) conducted a study on 461 women using various types of cu-IUCDs. A six month follow up of 236 women with initially normal smear had revealed high

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incidence of inflammation. This inflammation showed reduction by treatment. As consistent release of copper from the device has been reported in the uterine milieu as well as in cervical mucus by Hagenfeldt (1972), it seems that copper released in the mucus (which was quantitatively analysed by Hagenfeldt as 50% of the total amount of the metal released) somehow leads to the causation of inflammatory changes in the cervical epithelium.

Roy Chaudhury, etal (1980) conducted a study of vaginal cytological changes following use of different methods of contraception. They reported 9 cases of inflammation in 120 loop users, and 3 cases of inflammation in Copper 'T' users. The changes were evidenced within 7-12 months of use. 3 cases of women with opposite condom user partner showed inflammatory changes. Inflammatory changes in oral contraceptive users appeared after a long time of the use of the pills. Only 6 cases were seen having inflammation among 94 women. But in all cases there was a reduction in the incidence by treatment.

There was no evidence of carcinoma in any of the vaginal smears of women using different methods of contraception.

Study of Endometrium

Endometrial biopsy was done in women using different contraceptives at the 2nd visit at 9 months duration. This was done to see the effect of different contraceptives on the endometrium.

Endometrial biopsy was done in 100 women among the copper 'T' users. 84% cases showed a normal pattern. 6% cases showed stromal oedema. Only 2% cases showed chronic endometritis. 8 cases had an inadequate endometrium so opinion was possible in these cases.

In loop users, endometrial biopsy could only be done in 6 cases. 4 cases showed a normal endometrial histological pattern and 1 case showed stromal oedema and the other had an inadequate endometrium.

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In 36 women using oral contraceptives, endometrial biopsy was performed. 66.11% showed a normal endometrial pattern, 11.11% revealed cystic hyperplasia and chronic endometritis, 5.55% cases had stromal oedema and in 11.11% cases the endometrium was inadequate making the opinion impossible.

In 14 women with an opposite condom user partner, endometrial biopsy was done. All cases, except 2 with inadequate endometrium showed a normal histological pattern according to phase of the cycle.

In 12 cases of control, 8 showed a normal, proliferative and secretory phase. 2 had stromal oedema and 2 cases had an inadequate endometrium. There was no case of cervical or endometrial carcinoma through out the study.

With regard to the effect of IUCD on vagina, cervix and uterus so far there is no suggestion that incidence of cervical carcinoma is increased in women using such devices. The studies do, however, demonstrate the presence of abnormal cervical smears, although no statistically controlled studies on sizeable population have been done so as to compare the incidence of cervical dysplasia in general population as compared to that of IUCD using population. Moreover, the biological behaviour or cervical atypia in these two groups of population has also not been studies long enough to provide a reliable data.

The findings of the present work are practically similar to the observations of following workers.

Cervical neoplasia may develop at varying periods in women using Lippes loop as described by Mazgaliea (1964), Tietze (1966) and Tirhawar etal (1966).

In 1966 World Health Organization (WHO) Scientific group reported that histological studies on uteri of many hundreds of women, wearing intrauterine devices, had failed to reveal any changes related to neoplasia.

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Richart and Barrow (1967), analysed the progress of cervical dysplasia to carcinoma in situ in women having intrauterine devices and failed to find a significant difference from the control group.

Cytological studies of Schwartz etal (1967), Bagiroglu and coworkers (1970) had also failed to detect any evidence of preneoplastic or malignant changes in the cervical epithelium of women, retaining an Intrauterine Device for as long as 6 years.

Ishihara etal (1970) again in a cytological study in women using intrauterine devices reported suspicious smears in 68 (6.4%), out of 1058 women. But they had not reported any malignant changes in final histopathological diagnosis among 68 women.

Retrospective and Prospective studies had failed to support any carcinogenic action of copper upon the generative tract. Tatum (1973) studied serial Papanicolaou smears of the cervical epithelium. These he found to be normal over a period of use of copper 'T' for as long as 5 years.

In 1974, Tatum reported that aspirative endometrial biopsies from women who had worn a copper bearing 'T' for 5 years showed no greater incidence of endometrial hyperplasia or malignancy.

In 1977, Nishra and Coworkers in a cytological study in women, using copper intrauterine devices even for 4 years does not predispose to carcinogenesis in the cervix.

Ayre, etal (1966) studied 782 women during or after cyclic continuous oral contraceptive therapy. They concluded that there was no indication of carcinogenic influence even in pre-existing premalignant dysplasia of carcinoma in situ of the cervix.

Reid, etal (1966) found no significant atypical changes in the examination of female genital tract smears from 1,628 patients taking contraceptive hormones.

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Scpost (1968) in order to classify the possible cancerous effects of ovulation inhibitors carried out cytologic and colposcopic examination on 1,031 women who had taken ovulation inhibitors during 9,771 cycles. The histologically proven cervical carcinomas and epithelial atypias were found in routine examination of healthy women in the mass screening programme conducted by Rinehart etal (1956) who found 0.7% invasive and carcinoma in situ in women of all age groups.

Choudhary and coworkers (1980) also reported that although the original purpose of condom was to protect the user against venereal disease, if it is used together with medical contraceptives o like spermicidal jelly, some non-specific infection may result. In their study out of 44 cases of condom users there was cytological evidence of inflammation in 9 cases. All were non-specific inchracter. But there was not a single case where dysplastic changes or malignant changes were observed in vaginal cytology except 2 cases of mild dysplasia.

So it is evident from the present work that there is no precipitous carcinogenicity of modern contraceptives not even in the recently used oral pills or medicated. Rather, there is possibility of a prophylatic effect of these contraceptives controlling malignancy by restricting family.

CONCLUSION

CONCLUSION

In the present series 292 cases were studied regarding the study of clinical and vaginal cytological changes before and following the use of different methods of contraception.

The following temporary methods of contraception were chosen namely:-

(i) Intrauterine Cervical Devices mainly -
  (a) Lippes Loop
  (b) Copper 'T'
(ii) Oral Contraceptives.
(iii) Condom.

Though the number of cases studied does not form a large series yet the following conclusions are drawn:-

1. Majority of women using the different contraceptives were in the age range of 20-34 years. The youngest woman in the study of 20 years and the oldest was above 40 years.

2. These contraceptives were not only indicated for spacing but as a method of family limitation.

3. Mothers having 1 to 4 children were seen to use these contraceptives to the maximum.

4. Menorrhagia was the most common complaint of IUCD users. 46.71% women using Copper 'T' and 25.0% using loop had this complaint. 16% of oral contraceptives users developed menorrhagia.

5. Increase in weight have been observed in oral contraceptive users. No alteration was seen in weight in patients using IUCDs or conventional contraceptives.

6. Pelvic mass was present in IUCD users. 5.26% of incidence was reported in Copper 'T' users in the present study. there as it was not seen in Loop users probably due to the less number of cases in the present series.

7. Patients also complained of itching and vaginal

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discharge after the use of IUCD and conventional contraceptives.

8. A high failure rate of 13.33% in women with an opposite condom user partner and 6% with orals was observed. Only 2.6% of failure rate was seen in Copper 'T' users. A 5% failure rate has been evidenced in Loop users (as the number of cases was less in the present series.)

9. In 7.2% of women using Copper 'T' and 10% of women using Loop, the device had to be removed either due to pain or bleeding following the use of the device. 10% of women discontinued the use of oral pills due to pregnancy, forgetfulness or changes in weight.

10. 3.26% spontaneous expulsion were observed in Copper 'T' users. No case of expulsion was observed in Loop users.

11. The perforation rate of Copper 'T' was 2.63% and of Loop was 5% (due to less number of cases in the present study).

12. The Dysplastic changes were minly observed between 25 to 34 years of age range. Mostly Mild and Moderate grade of dysplasia was observed. Not a single case of severe dysplasia was seen in the present study. The dysplastic smears had accompanying infection, so patients were treated promptly. The inflamation was observed to subside by proper treatment and the dysplasia was also regressable. This was evident in the follow up vaginal smears.

21.05% of mild dysplasia and 1.31% of moderate dysplasia was observed in Copper 'T' users which regressed by treatment and only 10.52% of dysplasia was present at 9 months.

5 cases showing dysplastic changes in the Copper 'T' users did not take any treatment even then a regression to Negative smear was seen in 1 women and to Inflammatory smear in another woman. 3 cases was showed the same mild dysplastic changes.

1 case of the Loop users was not given any treatment. She showed a progression to moderate dysplasia.

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2 cases using oral contraceptives with dysplasia in their vaginal smears were not given any therapy. 1 woman did not show any change in her cytological pattern but the other woman showed a progression to moderate dysplasia.

1 case of the control group having mild dysplasia was also observed without giving any treatment. She showed a progression to moderate dysplasia.

In women using oral contraception 12.0% of mild dysplasia was present. These patients showed a slight increase in dysplastic changes at 3 months but again there was a regression to 6.0% at 9 months. No case of moderate or severe dysplasia was seen in oral contraceptive users.

Only 3.33% mild dysplasia was observed in women with an opposite condom user partner.

13. There was accompanying infection in the women having dysplasia. The inflammatory changes were non-specific and specific

14. Trichomonal infection was also present in women using different contraceptives. 13.76% of Trichomonal vaginitis was seen in Copper 'T' users, 40.0% was seen in oral contraceptive users and 15.0% was present in the control group. There was no evidence of Trichomonas in the Loop users as the number of cases in the series were less. This infection also responsed by prompt treatment.

15. Endometrial biopsy was also done at 9 months at the 2nd visit. In women using different contraceptives. Mostly patients had a normal secretory and proliferative endometrial pattern. In oral contraceptive users 61.11% women showed a normal pattern. 11.11% had cystic hyperplasia. 11.11% showed chronic endometritis. 5.55% women had stromal oedema and 11.11% had an inadequate endometrium in which no opinion was possible.

In 84.0% women of Copper 'T' users, a normal endometrial patternwas obtained. 2% had chronic endometritis and 4% had stromal oedema and in 8% inadequate endometrium was obtained, making an opinion difficult.

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4 cases showed a normal endometrial pattern in the Loop users out the 6 cases, and 1 had stromal oedema while in the other inadequate endometrium was obtained.

In 121 cases with opposite condom user partner, 12 showed a normal endometrial pattern and 2 had an inadequate endometrium.

16. There was no case of malignancy seen either in vaginal cytology or endometrial biopsy. So there was no association of the use of these devices with malignancy.

With all the above findings of the study there is no correlation between the use of different modern contraceptives to development of carcinoma of cervix and endometrium.

The dysplasia and inflammation which developed due to these contraceptives are reversible after discontinuation or removal of device. Dysplasia is reversible even when the Copper 'T' is in situ, as the copper coating provides a protective cover.

Failure rates due to pregnancy are more with oral contraceptives and condom users.

Spontaneous explusions are more in Copper 'T' as compared to Lippes Loop.

ABBREVIATIONS

ABBREVIATIONS

IUCD	.. ..	Intra-uterine Copper Devices
Cu	.. ..	Copper
Zn	.. ..	Zinc
FSH	.. ..	Follicular Stimulating Hormon
LH	.. ..	Luteinizing Hormone
GNRH	.. ..	Gonadotropin releasing harmone.
Fig.	.. ..	Figure.

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